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MARKETING THE USE OF THE SPACE ENVIRONMENT FOR THE PROCESSING OF BIOLOGICAL AND PHARMACEUTICAL MATERIALS

FINAL REPORT

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MARKETING THE USE OF THE SPACE ENVIRONMENT FOR THE PROCESSING OF BIOLOGICAL AND PHARMACEUTICAL MATERIALS

Final Report

Prepared for

The National Aeronautics and Space Administration
NASA HEADQUARTERS

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Prepared by

ECON, Inc.

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ABSTRACT

This study examines the perceptions of U.S. biotechnology and pharmaceutical companies concerning the potential use of the space environment for the processing of biological substances. Physical phenomena that may be important in space-based processing of biological materials are identified and discussed in the context of past and current experiment programs. The capabilities of NASA to support future research and development, and to engage in cooperative risk sharing programs with industry are discussed. Meetings were held with several biotechnology and pharmaceutical companies to provide data for an analysis of the attitudes and perceptions of these industries toward the use of the space environment. Recommendations are made for actions that might be taken by NASA to facilitate the marketing of the use of the space environment, and in particular the Space Shuttle, to the biotechnology and pharmaceutical industries.

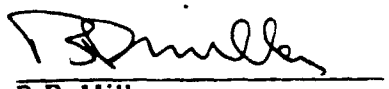
NOTE OF TRANSMITTAL

This study of approaches that might be used by NASA to market the use of the space environment to the biotechnology and pharmaceutical industries was performed for NASA Headquarters by ECON, Inc. Ms. Helene Najduk was the principal Technical Officer at NASA Headquarters for this study and Mr. Ray L. Gilbert was the alternate Technical Officer. ECON, Inc. is indebted to both Ms. Najduk and Mr. Gilbert for their assistance and guidance in this work.

The ECON Project Team for this study consisted of Mr. Ameen Ahmad, Dr. Edwin Dupnick, Ms. Carole Gaelick and Mr. B.P. Miller. Dr. Dupnick and Mr. Ahmad analyzed the capabilities of NASA to support research in the zero-g environment. Ms. Gaelick reviewed and documented the past and on-going work by NASA and others in the field of space bioprocessing, and performed the research that led to the selection of the industrial participants in this study. Mr. Miller developed the format for the meetings with the industrial participants, conducted the meetings with the assistance of Ms. Najduk and interpreted the results. Professor Dudley Saville of Princeton University assisted the Project Team in the analysis of separative technologies and in a review capacity.

A large number of industrial organizations and institutions also assisted in making this study a success. The American Institute of Aeronautics and Astronautics (AIAA) provided much useful information on individuals in the biotechnology and pharmaceutical industries who had been contacted through their various technology transfer activities. The Industrial Biotechnology Association and the Pharmaceutical Manufacturers Association assisted in the identification of the potential industrial participants. Most importantly, the study is indebted to the nine biotechnology and pharmaceutical companies that participated in the individual meetings. The information furnished by these companies formed the basis for the success of this study.

The interpretation of the results of the meetings with the biotechnology and pharmaceutical industries, the conclusions and recommendations drawn from their meetings, and the preparation of this final report was the responsibility of Mr. B.P. Miller.



B.P. Miller
President

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1. SUMMARY OF FINDINGS

Since the Apollo 14 flight in 1971, NASA has engaged in research, development and experimentation in the use of the space environment for the processing of biological materials. Experiments involving electrophoretic and isotachophoretic separation of biological materials were flown in the Apollo 14, 16, Skylab and Apollo-Soyuz missions. After a hiatus of nearly seven years, the flight experiments resumed under the auspices of NASA and McDonnell-Douglas Astronautics Company (MDAC) in the Space Shuttle in 1982. Although the experiment programs have continued with generally encouraging results for more than a decade, the commercial potential of space biological materials processing has not developed as rapidly as other space applications such as satellite telecommunications, meteorology or navigation. As a result, the demand for the use of the space environment by the biotechnology and pharmaceutical industries, and in particular the demand by these industries for the use of the Space Shuttle, remains uncertain.

The purpose of this study was to examine approaches that might be taken by NASA to market the use of the space environment to the biotechnology and pharmaceutical industries. Specific objectives included the assessment of the needs and attitudes of U.S. biotechnology and pharmaceutical companies concerning the use of the space environment, and the testing of the feasibility of a direct marketing approach for the use of space transportation to these companies.

The study was performed by identifying potential customers for the use of the space environment within the biotechnology and pharmaceutical industries. Meetings were then held with selected companies to gauge the state and sources of their knowledge concerning NASA and its programs in the space processing of

biological materials, NASA capabilities to support this research and the opportunities for cooperative research and development with NASA. Specially prepared briefing materials were used to generate and focus the discussion in these meetings.

Contact was established at the senior management level with 19 biotechnology and pharmaceutical companies, and meetings were held with nine of these companies. The meetings were generally informal, but were structured through the use of a presentation style report to obtain the information sought by this study. The results of the meetings were formally documented for subsequent analysis. The individual meeting reports, along with the presentation material used in these meetings are included as Appendices to this report.

The high level of industry participation that was obtained in this study, and the fact that all of the participating companies requested additional information and/or follow-up meetings, are both indicative of what appears to be a strong interest on the part of these companies in NASA and in the potential for the processing of biological materials in the space environment. However, a disconcerting result of these meetings is the apparent lack of information (and in some cases the presence of misinformation) concerning the NASA program. This problem is compounded by the fact that there does not seem to be an established process for NASA to convey information to these industries. For example, few of the industrial participants had specific knowledge concerning the separative research that is being conducted by NASA and MDAC. Even fewer were aware of the opportunities for cooperative research and development with NASA. By design, the participating companies in this study were chosen to exclude those biotechnology or pharmaceutical firms that were involved in a cooperative agreement with NASA or were participating in other NASA studies. Only three of the companies

interviewed had previously considered the use of the space environment. All three cited a lack of information or economics as factors in their negative decisions. It is interesting to note that none of the three took the step of discussing their preliminary thoughts on this subject with NASA. Several of the companies questioned the focus of the current space bioprocessing work on electrokinetic separation, and suggested other space biological research that might be promising. There was a widespread perception by the industrial participants that the cost of operating in the space environment was prohibitively high, and that cost would be an inhibiting factor in their future plans for space-based research, development or production. The reaction of the industry participants to a direct marketing approach was uniformly positive, and this type of marketing should be considered as a part of any future strategy that is developed by NASA for marketing the use of the space environment for the processing of biological materials.

On the basis of this study, it is recommended that:

- NASA provide follow-up to the specific action items such as the requests for additional information, meetings and speakers resulting from the meetings with the companies that participated in this study.
- A formal, long-term marketing plan be developed to provide for an on-going dialogue between NASA and the biological and pharmaceutical industries. Based upon the success in this study, direct marketing should be an integral part of their plan.
- The quality and quantity of information available to industry concerning the NASA program and the opportunities for cooperative research should be improved. Databases on subjects such as experiments, capabilities, facilities and experimental equipment would be useful in responding to requests for information by industry.
- Actions should be taken by NASA to remove some of the uncertainty concerning the costs of operations in the space environment. This should include the development and publication of policies for the use and pricing of those Space Shuttle payload areas where policies do not exist at the present time, and the development of pricing algorithms can be used by NASA customer representatives to provide pricing information to industry concerning these likely payload areas.

2. INTRODUCTION AND TECHNICAL BACKGROUND

Purification and separation of biological materials into their component parts is of great importance in certain biomedical fields.[1] Separation of biological materials on earth is accomplished by a variety of techniques including density gradient centrifugation, isoelectric focusing, filtration, absorption chromatography, electrophoresis and laser activated cell sorting. Problems are associated with each of these techniques and in some cases a number of techniques must be applied to achieve an acceptable separation.[2,3] In some of these procedures, particularly electrophoresis and isoelectric focusing, gravitational effects such as convection and sedimentation interfere with the separation process. Although techniques have been devised to prevent or suppress these effects on earth-based processing, these techniques are limited for cell and macromolecule separation and can be applied to separations of only small quantities of proteins. Therefore an increasing amount of attention has been devoted to the subject of biological separation procedures in the low gravity environment of space where convection and sedimentation can be avoided. A number of experiments, commencing with an electrophoresis experiment on Apollo 14, and continuing through the recent continuous flow electrophoresis experiments flown on the Shuttle by MDAC, have been carried out on-orbit. These have had their successes and failures, but a great deal has been learned and many expectations of the advantages of biological separations in space have been upheld.

2.1 Physical Phenomena Effects

2.1.1 Gravitationally Induced

Several phenomena caused by gravitational forces on earth including sedimentation, hydrostatic pressure and buoyancy-driven convection have detrimental

effects on some processing of materials.[1,4,5] Experimentation in a low gravity environment eliminates these gravitationally induced effects, and allows other forces such as surface tension, volume charge or spacecraft motion to predominate.

At one gravity mechanical stirring is required to keep large particles of different molecular weight and density in suspension. This stirring may be harmful to the separation process of chemical and biological separations and destructive to the chemical or biological species.[5,6] Sedimentation causes problems in ground-based electrophoresis, which will be addressed below, and procedures to circumvent these problems limit the rate of materials that may be processed. Under the low gravity conditions of space, components remain in suspension regardless of their densities.

Gravity creates hydrostatic pressure which causes materials to deform or collapse under their own weight. The absence of this pressure has implications for processing of certain alloys and crystals, and will eliminate the need to use a container to confine liquids and molten metals within a container. The materials will be held together by surface tension and may be controlled by use of acoustic, electromagnetic or electrostatic fields.[4,5] "Containerless processing" has the advantage of eliminating wall effects such as contamination, heterogenous nucleation, induced strain and nonuniform temperature distributions.[3,7]

Buoyancy-driven convection is a particularly tricky problem in the separation of biological materials. Temperature gradients result from the use of electric fields in electrophoretic separation. Because on earth the warmer portions of the fluid rises and the cooler portions settle, the separation process is disturbed by currents resulting from this motion.[7] Techniques have been devised to minimize, but not eliminate convective effects on earth.[3]

Sedimentation and convection severely limit the concentration and purity of the biological samples that can be separated on earth.[7]

2.1.2 Nongravitationally Induced

Another problem that has caused fluid flow distortion in earlier space experiments is the electrokinetic phenomena called electroosmosis. Electroosmosis is not dependent upon the presence of gravity, and has occurred in both the space and ground environments. When an external electrical field is applied to any system contained in a closed chamber with charged walls, electroosmosis as well as electrophoresis will occur.[8,9] Electroosmosis causes the solvent in which the particles are suspended to flow along the surface of the chamber in one direction and then return through the center of the chamber in the opposite direction.[8] This occurs because ions are absorbed by the walls of the tubes. These absorbed ions attract a layer of oppositely charged ions in the buffer. In an electric field, the layer of charge in the fluid moves, causing the buffer flow to move along the walls. This flow, when combined with the return flow in the center of the tube, produces a parabolic shaped flow. This phenomenon may be avoided if the walls are lined with an appropriate coating,[3,10] but coatings of "zero mobility" are difficult to synthesize and even harder to maintain.

2.2 Processes

Several separation processes have been identified as good candidates for space experimentation. Electrophoresis, isoelectric focusing, isotachophoresis and liquid phase partitioning are techniques that might be improved under low-gravity conditions.[3]

2.2.1 Electrophoresis

Electrophoresis is the transport of electrically charged particles under the influence of a direct current electrical field.[3,11,12,13] The process is useful for

separating different components of a mixture, because particles will migrate at different rates depending on their surface charge, towards an electrode with an opposite charge.[3,12,14,15] Most biological materials when dissolved or suspended in an aqueous solution acquire a characteristic electrical charge due to the ionization of their functional groups, ion adsorption or other phenomena[9,16,17] and their migration velocity per unit electric field (electrophoretic mobility of the substance) is fixed[17] in a given buffer. Electrophoretic mobility is a complex function of the particle's electric charge, molecular size, shape, hydration and all the characteristics of the solvent.[14,16]

The applications of electrophoresis may be broadly classified as: (1) identification and characterization of an ionized species, (2) determination of the quantitative composition of a complex mixture (3) actual separation of the components in a mixture. The procedure may be applied to the separations of proteins, complex macromolecules or colloids, cells, etc.

2.2.1.1 Static Electrophoresis

In static electrophoresis, materials that are to be separated are injected into a column of stationary fluid in an electric field. The materials migrate along the column according to their differing mobilities and separation occurs with time.[12,18]

A good separation is possible with static electrophoresis, but only a small amount of sample can be separated at one time. Therefore it is only used for analysis, not production.[18]

2.2.1.2 Continuous Flow Electrophoresis

For separation of larger or preparative quantities of material, continuous flow electrophoresis, which allows for continuous insertion of sample

and collection of fractions, may be the best method.[7,17,19] A curtain of buffer solution flows between two electrodes which establish a controlled voltage gradient.[6,18] A stream of sample material is continuously injected into the solution, which carries the sample from the top to bottom of a long rectangular chamber. As the material flows through the chamber an electric field is applied across the flow causing differently charged particles to deflect at an angle determined by the flow rate and electrophoretic mobility of the particles, splitting the sample into separate particle streams that exit out of separate outlets.[6,12,18]

2.2.1.3 Problems

Electrophoresis is subject to significant problems, many caused by gravity.[1,13,18] If the solute being separated is present in significantly high concentrations it will add to the density of the supporting electrolyte, and this density difference can result in gravity driven convection. Since concentrations of the material must be limited, the throughput is limited. Also, some solute particles may be sufficiently large to sediment.[13] Large biological particles of high density settle to the bottom of electrophoresis beds and cannot be effectively separated.[9]

Another complication in electrophoresis is that the electric field causes heating within the medium which, as noted above, can cause thermal convection in ground-based processing[14,21] producing flows that disrupt the movement of the particles and impair the quality of the separations. In earth-based processing the spacing between the front and rear walls of the chamber must be very small to minimize the temperature rise caused by the current and prevent convective perturbations from thermal gradients. This limits throughput because it allows only a small sample stream and permits distortions from wall effects that degrade

the resolution of the device. The applied field may be limited to reduce heating and prevent convective circulation from nonvertical temperature gradients existing because of heat transfer to the wall. Unfortunately this restricts the degree of separation that can be obtained.[3]

Another problem, known as bandspreading, is caused by several factors including differences in density between the buffer fluid and the biological stream, electroosmosis, differences in residence time and force that causes differential migration of the sample. Those particles closer to the center of the stream are in the electric field a shorter time and move shorter lateral distances. The particle mobility is thus dependent to some extent on its location in the chamber. Bandspreading prevents the streams from completely separating and limits the purity of the output.[7,12] Bandspreading may be eliminated in space if a thick enough chamber is designed.

In a low gravity environment resolution and volumetric throughput should be vastly improved, although secondary convective effects which are obscured in one gravity may impose finite constraints on the achievement of theoretical maxima.[14]

2.2.1.4 Electrophoresis of Cells

Isolation of functionally pure subpopulations of living cells is of central importance to research work in immunology, cancer and other therapeutic areas.[22] Also, pure populations of cells could be implanted into patients with a deficiency of that particular cell. For instance pure beta cells could be transplanted into diabetics, and the stem cell into persons suffering from neoplasia of the bone marrow.[5,15,22]

The efficiency of cell culturing processes could be enhanced and commercial production of valuable substances made possible by separating cells into purer subfractions that have a high production rate of the substance of interest, for culturing.[1,5,15,22] Experiments have shown that production of the enzyme urokinase is higher in certain subpopulations of kidney cells, and the more productive cells could be separated by electrophoresis.

Unfortunately, most conventional separation techniques are inadequate in isolating cells according to function because they are based on characteristics such as size, density, and appearance which may be similar in cells that differ in function. Or they are based on characteristics that are so specific that they can only be used on previously purified cell populations.[1,5] Some powerful non-electrophoretic techniques for cell separation now exist such as electrostatic cell sorting, sedimentation techniques, affinity chromatography, phase partition with polymer systems and others. But inherent problems exist with ground based electrophoretic techniques for cell separations, including poor resolution of the continuous flow apparatus, sedimentation and artifacts due to polymeric materials in density stabilization.[22] However, continuous flow electrophoresis and phase partitioning (defined below) avoid these restrictions, and may be used to separate materials into groups that are biologically meaningful.[1] Both of these methods are impaired by gravity-driven effects. Continuous flow electrophoresis is impaired by sedimentation and convection as was described above and phase partitioning by sedimentation as will be described below.

Some restrictions on cell separation may be minimized by using vertical columns with a density gradient to stabilize the fluid against buoyancy-induced convection, although sedimentation remains a problem with this technique.[1,19]

Horizontally oriented columns rotated slowly minimize sedimentation effects.[19] Thermal convection can be reduced by applying low electric fields, but this slows the separation.

Most of the information on cell electrophoresis has been provided by microscope electrophoresis (static electrophoresis). This analytical technique requires the direct observation of the migration of individual cells under a microscope. It is a slow and tedious method and fortunately is being replaced by techniques for rapid electrophoretic mobility determination.[11,16] During the microscopic measurement of cell mobilities thin wall capillaries are horizontally oriented.[19] Because the applied electric field is low, and the capillaries are immersed in a temperature controlled water bath, thermal convection is small. Sedimentation is perpendicular to the electrophoretic migration and essentially limits the duration of the mobility measurement.

Although column electrophoresis has only had limited success on the ground, it is a first choice for space where the fluid could be uniform and stationary with no disturbance due to buoyancy-induced convection or sedimentation.[1,19] Significant advances in the performance of electrophoresis could be attained by carrying it out in space.[1]

General areas in cell biology that could benefit from bioprocessing in space are:

- The study of particular enzymatic and transport processes that are localized to specific areas of the cell by isolating from crude cell homogenates the membrane fraction that contains the substance of interest
- The study of the activity of molecules that are usually hidden on the inner surface of cell membranes by separating the inside out from the outside out membrane vesicles[4]

- Improved selection of cells for tissue culture production of biologicals and vaccines
- Cell purification for direct cell therapy for treatment of immune deficiencies.[16]

Cell electrophoresis has profited from research using ground based techniques and this advance in knowledge will permit space research to be better focused. Laser techniques and computer controlled television camera based apparatus for automated microscope electrophoresis are providing fast means to obtain data on cell populations. Work remains to be done in establishing the relationship between cell mobilities and various cell functions such as immunologic, metabolic, synthetic, and physiologic activities. Another problem is that some cell subpopulations such as T and B lymphocytes have overlapping cell mobilities and therefore are not completely separable by electrophoresis.[23]

2.2.1.5 Protein Electrophoresis

Protein electrophoresis on the other hand, is a mature technology with a number of established ground based techniques available for analytical or micro-preparative work.[11,16,23]

Convective mixing brought on by the Joule heating is the principal limitation of the use of electrophoresis for protein fractionation. Porous gels are used to suppress the mixing.[8,19] In addition, the supporting gel matrix provides an element of molecular sieving on the separation process.[11] Unfortunately the gel restricts quantities that can be separated, complicates the extraction of the fractions, and is not useful for biological cells and particles.[19]

The use of these techniques appears to be satisfactory for analytical and micropreparative electrophoresis of proteins. However, the procedures are not applicable to large particles such as cells, and it has not yet been possible to scale up the instruments to produce commercially significant quantities of proteins.[16]

This is because most instruments carry out two functions: the separative function and the Joule heat dissipation function. Heat dissipation is through the walls of the vessels and is proportional to the square of the radius while the capacity of the instrument, and therefore the Joule heat generated, is a function of the cube of the radius.[23] Access to a low gravity facility may provide a breakthough by allowing the use of instruments designed for the weightless environment that separate these two functions.[11,23]

2.2.2 Isoelectric Focusing

Unlike electrophoresis, isoelectric focusing, is not a rate process, but an equilibrium one. Isoelectric focusing utilizes a voltage gradient to set up a pH gradient in the buffer solution. Mobility of the particle varies as a function of the pH of the buffer. There is a value of pH, known as the isoelectric point at which the particle's mobility is zero. Particles migrate to their isoelectric points and remain there becoming virtually immobilized. It is possible to achieve high resolutions with this process because the boundaries of the sample band are self-sharpening. Because the focusing process counteracts diffusion the method is particularly useful for proteins and other macromolecule separation. Isoelectric focusing is effected by sedimentation problems and gravity-induced convection.[1,3,15,18,24] Even slight electroosmosis can severely effect the isoelectric focusing process because the components mobilities are approaching zero as the proteins approach their isoelectric point. The closer the proteins are to this point the more drastic the effect of electroosmosis.[24] A novel isoelectric focusing machine has been developed for possible use in space by Dr. Milan Bier of the University of Arizona.[1]

2.2.3 Isotachophoresis

Isotachophoresis differs from ordinary electrophoresis in that the sample is inserted between two buffers. The leading buffer's anions have greater electrophoretic mobility than the sample, and the trailing buffer's anions have less mobility. When voltage is applied, the different compounds tend to form sharp distinct bands according to the mobility of the anions. Bands progress at equal velocity through the column and over the course of migration sample ions are arranged in order of decreasing mobility. The main advantage of the technique is that any molecule that diffuses across the interface is automatically returned to that region corresponding to its mobility.[3,15,25] If convective mixing could be alleviated this method could produce extremely high resolution.[3] The technique needs a method of recovery if continuous operation is desired.

2.2.4 Phase Separation

Phase separation, or countercurrent distribution could also be improved in a low-gravity environment where sedimentation is greatly reduced. In this technique, cells that are to be separated are mixed with two immisible liquids. Depending on its surface properties, the cell usually shows a preference for one phase over the other. On earth sedimentation interferes with separation because the droplets sediment before the partitioning reaches equilibrium.[3,18] Because sedimentation is reduced in space a stable liquid suspension can be maintained long enough to achieve full partitioning. An electric field must be applied across the fluid to induce separation, since the phases do not readily separate.[18] This technique is much less developed than electrophoresis.

2.3 Space Experiments

2.3.1 Apollo 14 Experiment

On-orbit electrophoresis experimentation began in early 1971 when an electrophoresis demonstration was performed aboard Apollo 14 on its return trip from the moon.[5]

The three materials selected; red and blue dye mixture, hemoglobin, and salmon sperm DNA,[21,26] represented a broad range of molecular weights.[27] The experiment was composed of three electrophoretic columns containing a borate buffer. The goal was to observe the shape and distortions of the sample band as it moved under the influence of the applied field.[3] Data were acquired by photography, and there was no attempt to collect the separated fractions.[3,21]

Poor lighting and camera positioning problems impaired photographic quality, but the separation of red and blue dyes was discernable in the photography.[3,27] Densitometer measurements made on the photos indicated that the boundary between the dyes was sharper and better defined than that obtainable in a liquid column under similar conditions on earth. Photographs taken of the space experiment did not show lateral motion due to thermal convection or sedimentation as is evident in similar experiments performed on earth.[26]

But electroosmotic flow along the column caused severe distortion of the shape of the sample band.[3] Electroosmotic band-broadening would have been considerably less severe had there not been a slide valve misfunction. A slide valve that did not fully open put the dye sample in the region of maximum electro-osmotic shear, rather than in the center of the tube where electroosmotic band broadening would have been one third as great.[26]

There was no trace of the two biological samples left in the apparatus, they were apparently destroyed by bacteria in the system, probably during the long

storage period before the demonstration took place.[21,27,28] The unit itself worked as designed and was later reused on other flights.[9,27,28]

2.3.2 Apollo 16 Electrophoresis Experiment

A second experiment was carried out on board Apollo 16 in 1972 using an apparatus similar in size and shape to that used on Apollo 14. Alterations were made in the photographic setup. Photographs were automatically taken every 20 seconds during the separation run and again there was no attempt to collect samples. The photos and astronauts' commentary were the only data.[28] The sample injection system was redesigned to provide a smoother and more reliable release of samples.[21]

One sample material, monodisperse polystyrene latex particles (PSL) were used in three separation columns. The first column had a mixture of particles of 0.2 and 0.8 μm diameter, and each of the other two contained particles of the same diameter (either 0.2 or 0.8 μm) to provide comparative data. The material was chosen because its electrophoretic mobility is well known, and because it is not subject to bacterial degradation [21,27] and could serve as a model for live biological materials.[17,28]

Ground based work using sucrose solution density gradients was used for comparative purposes[27,28] and an actual comparison did indicate the possible improvements in electrophoretic separation.[27] No convection occurred during the space experiment[21] but there were problems with electroosmotic flow and bubbles.

The sample was injected as a cylindrical disk, but by the time the particles were visible in the photos the front of each group was already parabolic due to electroosmosis (less than 0.5 cm from the sample input).[9,21] Electroosmosis is the result of high zeta potential on the walls of electrophoretic chambers. At the time of this experiment there was no low zeta potential coating available that would adequately adhere to chamber walls.[28] Had this been available, electroosmosis

could have been reduced and a distinct separation of the two sizes of latex spheres achieved.[28] When the sample was exposed to the cell buffer and electric field, bubbles that were motionless before electrophoresis began, starting migrating with constant velocity towards the anode.[9]

The cause of the bubbles was attributed to the permeability of the silicon tubing--expecially since it was subjected to the rapid external depressurization of an Apollo flight.[27]

A slight separation of the latex sphere mixture containing the two different sized particles was distinguishable using very sensitive photographic techniques[5,9,28] despite the distortion produced by electroosmosis.[3]

Fluid disturbances also developed causing one of the migrating zones to take on a corkscrew appearance. No definitive explanation is available, but it has been suggested that the disturbances may have been caused by spacecraft motion, or thermal or electrical gradients in the fluid.[17]

Although problems with electroosmosis, bubbles and fluid disturbances did occur, electrophoresis was accomplished and[28] the experiment proved conclusively the advantages of zero gravity in eliminating convection caused by density differences. To avoid these difficulties in the future, a certain stabilization of the fluid may be necessary. Isoelectric focusing (with protein electrophoresis) or isotachophoresis both have built-in self-stabilization of boundaries.[17]

2.3.3 Apollo-Soyuz Experiment MA-011

Experiment MA-011 (1975) was a static electrophoresis system that was designed for high resolution and for testing various electrokinetic techniques such as isoelectric focusing and isotachophoresis.[7,29]

The equipment developed for the Apollo experiments was extended and combined with new sample handling procedures to work with biological materials.[30]

Some of the objectives of this experiment were to:

- Separate and return viable lymphocyte and kidney cell fractions[21]
- To test the effectiveness of a low-zeta potential column coating, in eliminating electroosmosis
- Demonstrate the isotachophoresis of cells in space
- Preserve the isolation and viability of biological samples after electrophoresis
- Evaluate and analyze the resolution and sharpness of the band formed by free zone electrophoresis in space
- Test the space-rated static electrophoresis apparatus.[21,25]

The experiment used eight sample insertion slides, two of each of the following:

- A mixture of aldehyde fixed red blood cells from human, rabbit and horse,
- Human peripheral blood lymphocytes,
- Human fetal kidney cells,
- Rabbit and human red blood cells, one column fixed and one column frozen, which were used for the isotachophoresis experiment.[11,25,29]

The samples were frozen in liquid nitrogen until use and at the end of the run the columns were frozen in-situ and returned to Earth in liquid nitrogen.[3,11]

Overall, the equipment worked essentially as expected, although the experiment could not be deemed a total success because fluid lines in some of the columns were blocked. It would have been impossible to check these before flight without contaminating the enclosed sterile buffer.[25]

The problems of bacterial degradation of biological samples experienced on Apollo 14 and electroosmosis experienced on Apollo 16 were eliminated.[21] Electroosmosis was avoided because the inner walls of the tubes were coated with a suitable zero-surface-potential material.[25,29]

2.3.3.1 Results of the Separation Experiments

Aldehyde Fixed Red Blood Cells

Fixed red blood cells were chosen to demonstrate the separation capability of the unit because they are used as standard particles in analytical particle electrophoresis of biolcgical cells and extensive data on the electrophoretic mobility measurements of red blood cells in various buffers has been published. Also, the red cells used (erythrocytes fixed in formaldehyde) are an almost indestructible sample material resistant to mechanical stress, hemolytic agents, and surface modifications. Another reason for this choice is that the cells are visible to the naked eye at the concentrations used in the experiment and therefore can be photographed. Rabbit, human and horse red blood cells were selected because the mean mobilities of the nearest neighbor populations were separated by about 0.4 μ m s^{-1} V^{-1} cm so a successful separation would not be insignificant.[25,29]

The experiment achieved separations with sharp particle band boundaries. Generally the data showed the observed migration agreed with the predicted migration, overall the band pattern was a bit more compressed than expected and the separation between horse and human cells was greater than had been hoped for. Also the rabbit cells had greater mobility in space than was predicted and overlapped with the human cells more than was expected.[3,25,31] Twenty flight photos taken at three minute intervals did not reveal any band spreading or curvature due to electroosmosis.[25,31]

As one frozen cylinder (column one) was being sliced after its return to earth the column wall fractured and the cylinder was distorted. The slices were saved in the hopes that minimal contamination and mixing had occurred. Partial separation of cells of the three species according to electrophoretic mobilities was

evident.[25] The experiment, in the case of the other column (column five) did not function correctly because of a blocked electrode buffer circulation port which probably caused a fluid flow through the electrophoresis column which opposed the direction of particle migration and carried electrolysis products into the column.[25,31] This was the likely cause of the column having a pH range of 6.0 to 9.2. Separation occurred with this sample according to red cell species, but not to the extent to show distinct bands in the photographs.[25] There were two specific instances of sudden disruption of boundaries in the flight photographs, that may have been caused by random motion of the apparatus or the spacecraft.[31]

In the first column, the recovery of cells was 75 percent of the theoretical value, while in the second column it was 93 percent.[25,31] Data collected from 100 cells in each of three sample slices from each column were analyzed to determine whether they showed the electrophoretic mobilities that would be expected from their locations in the column.[25,31] Estimates made of the number of each cell type from the electrophoretic mobility data were in general agreement with the morphological typing estimations (for column five). In column one however, the three sample slices all had similar electrophoretic mobilities and did not display the expected trends. This supported the possibility that the samples had been mixed or contaminated when the column broke or had been mixed before freezing.[31]

Human Peripheral Blood Lymphocytes

Lymphocytes serve a recognized role in immunological responses to foreign protein antigens and foreign tissue. Because of the increasing emphasis on cellular interactions and the cellular basis of immunology, simple techniques to acquire pure fractions of lymphocytes from heterogenous cell populations have been in demand.[25,31] Electrophoresis was performed on two columns (columns two and six)

containing human peripheral blood lymphocytes in the MA-011 experiments. The following problems precluded the acquisition of adequate data.

Fluid line blockages caused gas bubbles to form around the electrodes in one column (column two) which caused the length of time the current was established to be cut short and therefore precluded migration of the lymphocytes.[25,29]

In the other column, (column six) current ran for close to 30 minutes but a blockage of some electrode chamber fluid lines caused an acid pH throughout the column that was 2.54 on the left, 2.28 in the center and 2.21 on the right resulting in only a one percent viability of the returned lymphocytes.[25,31] Viability of the returned cells in column two was six percent, and in column six was essentially zero percent.[25]

Human Fetal Kidney Cells

Human fetal kidney cells produce the enzyme urokinase which is used to dissolve blood clots. To produce this enzyme for therapeutic purposes kidney cells are grown out in cultures on mass tissue propagators from which the urokinase is harvested. Only five percent of cells in the kidney cortex produce this enzyme. Isolation of these urokinase producing cells could substantially increase the yield of urokinase from the cultures. That and the fact that ground-based work with separation techniques has shown a loss of resolution due to sedimentation of the large cells and convective mixing caused by Joule heating made this an ideal candidate for space electrophoresis.[25,31]

Results from the experiment supported the contention that these product specific cells could be separated. Viable cells were separated in orbit and cultured upon return to earth. One fraction, after being grown in culture on earth achieved a six-fold increase in urokinase beyond what any earth based technique has achieved.[3,25,29,30,31]

In another band human granulocyte stimulating hormone was the chief product of the cells, and yet another showed enhanced production of erythropoietin, indicating that these products are probably produced by different type kidney cells.[3,25]

These samples were taken from only one of the two columns because the other column developed a leak during processing.[3]

Isotachophoresis of Rabbit and Human Red Blood Cells

In isotachophoresis the boundaries between species of different mobility are sharply defined and stabilized by electrical forces. These boundaries will reform if disturbed. Once separation has been achieved the concentration of each substance within a compartment is uniform and remains constant throughout the run. Because of this, higher concentrations of components can be handled with no deterioration of the sharp boundaries. Sample compartments are contiguous to each other and never separate to form an intermediate zone of clean buffer. In order to achieve separation a "spacer ion" of the right intermediate mobility has to be added.

Gravity effects are more difficult to overcome than in zone electrophoresis because of the sharpness of isotachophoretic boundaries which give rise to steep concentration (i.e. density gradients). For this reason, protein isotachophoresis in a unit-g environment is always conducted in gels. When planning for the ASTP experiment began there was no ground-based apparatus in which cell isotachophoresis could be carried out. A new apparatus for cell isotachophoresis was developed after extensive ground based research only six months before the flight. The lead time for preparation of the experiment was not long enough for as thorough an evaluation as would have been desired.[31]

Isotachophoresis was performed on one column containing a mixture of frozen native rabbit and human erythrocytes and another column containing formalin-fixed human and rabbit red cells.

In the experiment with the fixed red cells, the photography was not good enough to show the whole column length. Only four frames were available for evaluation. The frontal boundary moved ten mm in nine minutes, confirming the predicted velocity,[25] although overall migration appeared to be somewhat lower than expected[21,31] and the boundary was flat and sharp as expected in isotachophoresis with an antiosmotic coating.[21,25]

In the column with the native unfixed red cells the overall migration distance was only 60 percent of what was expected.[25,31] Only the last four photographs of this column showed any trace of the sample.[25]

Separation between species of red cells was not observed in either column and because of insufficient migration distance the rear boundaries were not seen, and it was not possible to draw conclusions concerning separation.[25] The insufficient duration of the run (45 minutes) prevented the isotachophoretic bands from coming into full view.[21,31]

However, the experiment demonstrated the advantage of isotachophoresis in the sharpness of the frontal boundary and concentration of the migrating zones. The primary advantage of isotachophoresis is the potential quality of sample it may separate. In the case of cells the future of this process depends on finding proper spacers.[31]

2.3.3.2 Summary Comments--MA 011 Experiments

In spite of the fact that engineering and operational problems compromised six of the eight runs attempted, the experiment showed that space electrophoresis can provide capabilities not available on earth. MA-011

demonstrated satisfactory sample collection, return, and preservation techniques. Postflight analysis of the successful red blood cell separation and postflight analysis of a separation of cortical kidney cells show the apparatus successfully transported samples over distances of about ten cm without serious disturbances from fluid flow, a capability possessed by no earth based apparatus.[25,30] Progress in the development of bioprocessing was achieved by the application of near-zero zeta potential interior wall coating on columns to prevent electroosmosis, confirmation of biocompatibility of all appropriate hardware components and the use of a sterile operating environment.[25,31] The electrophoresis unit allowed for two different types of separations to be conducted and allowed for multiple runs. Not only were eight different columns processed, but the requirements for cooling, freezing, current, fluid connections and run time were varied in orbit.[31]

2.3.4 Apollo Soyuz MA-014

This experiment sponsored by West Germany was designed to perform continuous flow electrophoresis in space on biological cell materials with the goal of achieving high sample throughputs at high resolution.[6] The machine was designed to work almost automatically. There was no sample collection because of volume limitations for the instruments. Instead, the results were evaluated by scanning the absorption pattern across the separation gap, digitizing the data and storing both the scientific and housekeeping data on tape.[3,6,29]

In addition to demonstrating continuous flow electrophoresis at zero gravity for the separation of preparative quantities of living cells at high viability percentage, an objective was to investigate thermal and convective properties of chambers with high gap width.[6]

Samples that were separated were:

- Rat bone-marrow cells
- Rat spleen cells
- Mixture of human and rabbit erythrocytes
- Rat lymph-node cells and human erythrocytes.[29]

The first three samples were freshly prepared and stored at 4°C for about 45 hours preceding the experiment. The rat lymph node cells were stored at -85°C in liquid nitrogen.[6,29]

The tape-stored data was examined several days after splashdown. Proper running of all functional blocks was confirmed but scientific data indicated that the light source (a halogen lamp) for the absorption measuring optics had been excessively bright and adversely affected the measuring range. The reason was the lamp lacked internal convection because of zero gravity.[3,18,29]

Consequently it was difficult to interpret the recorded data. However, some conclusions were possible because during the stationary phase irregularly occurring pulses (called events) were recorded. The pattern of these events reflected the expected course of the separation curves.[6,29] It was concluded that:

- The bone marrow sample showed an excellent separation pattern, sharper than that measured by comparable ground equipment
- The best results were achieved with spleen cells. There was sufficient data to identify the details of the separation and the prediction of high separation quality in spite of high-rate sample processing was confirmed
- Well founded results from the erythrocyte separation were precluded by lack of information
- Lymph node cells showed a somewhat poorer distribution due to the lack of information stored,[29] but compared to the results of procedures carried out on the ground the positive effect of the absence of gravity was striking.[6]

2.3.5 Skylab-Experiment TV117

An attempt was made to separate human red blood cells and two proteins, ferritin and hemoglobin using isotachophoresis on Skylab. The objective was to determine whether low gravity could alleviate convective mixing and sedimentation problems that are associated with separations in one-gravity and achieve protein separations to compare with gel techniques, and to determine whether larger particles such as cells could be separated by this process.

The protein separation failed. A small amount of air had entered the system through slight leaks that had developed. A gas bubble formed and isolated the electrode, preventing current from flowing.

The tube with red blood cells produced better results, although the process was effected by electroosmosis.[3]

2.3.6 The Shuttle Era

Space experiments with electrokinetic separation of biological materials began in 1971 in the Apollo 14 flight and were continued at an increasing level of activity and sophistication through the completion of the Apollo-Soyuz mission in 1975. Because of the hiatus in the manned space flight program, flight experiments using separative technology did not resume until the flight of STS-1 in 1982. In the intervening seven years an important action occurred that could eventually lead to a private sector role in the commercial development of the space environment for the processing of biological materials. In 1976 MDAC began the development with their own funds of a continuous flow electrophoresis device. In 1980 MDAC signed a Joint Endeavor Agreement (JEA) with NASA to establish a cooperative research and development program. Under this program MDAC would conduct certain proprietary precommercial electrophoresis separation experiments in the NASA Space Shuttle. Under the terms of the JEA, NASA agreed to provide

MDAC with transportation of the electrophoresis unit to and from orbit at no cost to MDAC and further agreed that it would not accord similar privileges to other private sector entities proposing to conduct experiments in continuous flow electrophoresis. In turn, MDAC agreed to support the NASA in-house research program in space bioprocessing by conducting separative experiments in their continuous flow electrophoresis device with material samples provided by NASA. In addition, NASA sponsored the development of a static electrophoresis device for flight in the Shuttle and the development of a isoelectric focusing device for ground testing and possible future flight.

With the flight frequency of the Shuttle increasing to nearly ten times per year in 1984 and 1985, in comparison to manned space flight opportunities of about once per year in the early 1970s, it is apparent that the era of the Space Shuttle has created an opportunity for a vigorous space bioprocessing program.

2.3.6.1 Industry Participation in Space Bioprocessing--McDonnell Douglas and Johnson & Johnson*

MDAC began investigating the prospect of space manufacturing in 1976. After several areas were considered, electrophoresis was chosen when the company recognized that the process had never been optimized on earth because of gravity induced limitations. Of primary interest was the fact that it appeared the process could be scaled up in space to allow large commercial quantities of materials to be separated, a capability that is not attainable on earth. By 1977 the company had formulated the program, and then it approached several pharmaceutical companies to determine the degree of interest in the possibilities of using space to produce new products. In 1978 a working arrangement was established

*The information contained in this section was obtained from various trade press sources, an interview with Mr. James Rose and Ms. Lynn Hansen of MDAC on November 1983 and an interview with Dr. Glenn Kiplinger of Johnson & Johnson on December 1983.

with the Ortho Pharmaceutical Corporation, a subsidiary of Johnson & Johnson (J&J).

Under the arrangement each company contributes in its area of expertise. MDAC has developed the equipment, does the space processing and ground analysis and ships the material to J&J. J&J has done the market research and product selection, will perform animal and clinical testing, decide the dosage forms, and will package and distribute the resultant product.

MDAC intends to market their space based electrokinetic separation technology and services internationally, eventually working on processing multiple products for a number of companies. The growth of this industry depends to a large degree on decisions made requiring future on-orbit capability. MDAC has indicated that it may be possible to process one or a limited number of products using the Space Shuttle and unmanned spacecraft. But for a multifaceted expansion the company is looking to the manned space station. According to MDAC a permanent manned capability in space is required for them to perform research in space, allowing for the expansion of the number of space produced products. Without the space station the industry will be limited to a few products.

According to MDAC the present space transportation system is being used for verification of processes and eventual production of products. MDAC has developed a ground-based processing system and a sophisticated mathematical model that analyzes the effects of gravity and can determine which processes are gravity limited and the magnitude of these limitations. From their ground work a strong database has been built, so they know what to look for and what to test for. On the basis of this ground based work a few samples are chosen for verification through space processing. If manned access to the space environment were unlimited, as would be the case if a manned space station was available, the

researcher could routinely run the experiments and research could be performed in space on hundreds of products.

MDAC has given glowing reports of its space-based work to date. Separations have been run on STS-4, 6 and 8. These runs have established that the process works significantly better in terms of throughput and resolution in space than on the ground. So far, one proprietary material has been prepared and beta cells have been successfully separated from living pancreas cells. Electrophoresis of kidney cells done for NASA produced a new plasmagin activator, an important enzyme that may be used to dissolve blood clots. This substance had never been separated on the ground because it was not possible to attain sufficient concentration of material required. Yields up to 700 times greater and purity levels four times higher than are achievable on the Earth have been attained by these runs.

On STS-4 the MDAC device was used to perform separations on a laboratory standard mixture of egg albumin and rat albumin and a cell culture fluid containing many types of protein.[32] The maximum concentration of albumen that can be separated on the ground is 0.2 percent which is insufficient for commercial purposes. A 25 percent concentration was achieved in the space experiment. This yielded about 460 times more material than is possible on the ground. Comparable success was achieved in the separation of tissue culture media.[33,37]

The device was flown again on the next two Shuttle flights and accomplished separation of over 700 times more materials and achieved purity levels more than four times greater than that possible on earth.[34]

In the STS-8 flight the MDAC continuous flow electrophoresis device was used to investigate the handling of live cells before and after processing and establishing the capabilities of the device to improve electrophoretic separation of live cells in space. Live pancreas cells were separated and survived the

experiment. Because of the cells sensitivity to bacterial contamination they were loaded into the on-board storage area only seven hours before lift off.[35]

There are indications that the test yielded separation rates at about the levels projected but more time is required to determine whether the cells are still able to produce hormones and enzymes as anticipated.[36]

The prospect of substantially increased yield from space-based processing appears to be a major driver behind the plans for commercial production. A new production plant, a scaled up version of the unit flown by MDAC in 1982 and 1983 is scheduled for first flight on the Shuttle in 1985, and is now being developed. The apparatus will be automatic and have twenty-four times the capacity of the current unit. It would take 16,000 columns on the ground to achieve the quantities that will be separated by the production plant in space.

Two flights are scheduled in 1985, on STS-51-I (i.e., flight number 27) and STS-61-C (flight number 32). These will be the first production runs, meaning that the returned product will undergo preclinical tests.

A modified machine will be used and payload specialists will be present on these flights. MDAC has indicated that is is their intent to have enough test data on products to get FDA approval for commercial sales by 1987.

An important observation made by MDAC about their venture with J&J is that it takes a combination of different groups and talents. MDAC, the initiator of the endeavor, possesses a unique set of capabilities including expertise and experience in the aerospace field, an active aerospace medicine department and the foresight to see beyond the typical short term investment horizon. J&J understands the market and has the knowledge and skills required to market the product. Washington University, which has done extensive work on beta cells and is involved in a joint research quest with MDAC which could lead to new treatments

for diabetes, has the theoretical research capability. The beta cell separation on STS-8 was part of this joint work. NASA provides access to the space environment on the Space Shuttle. From the perspective of MDAC all of these ingredients are needed for a successful program of experimentation and product development.

NASA will play a crucial role in influencing industry participation in space processing. Industry must be assured they can depend on NASA providing a reliable and efficient transportation system available routinely for industry use. The lead time in developing hardware and ground based research can be long, on the order of ten years or more. One of the concerns voiced by MDAC is the lack of commitment on the part of government to ensure continued Shuttle availability. In order to make a return on an investment in space processing, industry is dependent on long-term and routine availability of the Shuttle, and before it will undertake investments with a long return horizon industry must be certain the system will be there to support their work. A lack of commitment on the part of the government increases the risks and uncertainities that are perceived by industry in association with a space processing project. A national policy committing the Shuttle fleet to support commercial work may have an important effect on industry decisions regarding whether or not to venture into space processing.

2.3.6.2 NASA Sponsored Research

In addition to the industry program, NASA has continued the development of an active in-house space bioprocessing program as a part of the scientific utilization of the STS. This program has led to the development of a static electrophoresis device which was flown on STS-3, and an isoelectric focusing machine which is scheduled for flight in 1984 or 1985.

The static electrophoresis experiment in STS-3, called the EEVT, had as its goal the investigation of the electrophoretic behavior of animal cells in suspension that is more concentrated than that possible on earth. The samples consisted of six human embryonic kidney (HEK) cell cultures and two mixtures of human and rabbit aldehyde-fixed red blood cells. The comparison of laboratory results with the STS-3 results indicates that very high cell concentration is possible in zero gravity electrophoresis, and the results are not unexpectedly different from the electrophoresis of normal cell concentrations at unit gravity.[38]

The isoelectric focusing machine under development by Dr. Milon Bier at the University of Arizona differs in a very significant way from the MDAC and NASA electrophoresis devices. While the goal of electrophoresis is to achieve improved throughput, the objective of the University of Arizona isoelectric focusing machine is increased resolution. Laboratory tests of the University of Arizona isoelectric focusing machine have been encouraging and it is tentatively scheduled to fly in the Shuttle in 1984. Assuming that the MDAC continuous flow electrohphoresis machine is capable of providing adequate resolution with increased throughput, and that the University of Arizona isoelectric focusing machine is capable of achieving in space adequate throughput with increased resolution, in the present stage of research and development the two machines are very likely to be complimentary rather than competitive.[39]

2.4 Understanding the Potential Needs of the Biotechnology and Pharmaceutical Industries

With the successful completion of its tenth flight during the period of performance of this study in early 1984, the NASA Space Shuttle has demonstrated the reliability and reproducibility of performance of an operational system. The Shuttle will move further in the direction of full operational capability with eight to ten flights planned for 1984, and ten to 12 flights planned for 1985. By the end

of 1985 all four Shuttle Orbiters will be in full use. The capability of the Shuttle to revisit an orbiting spacecraft for retrieval, repair or replenishment of consumables will be demonstrated in 1984 and again in 1985. By the latter part of this decade the flight rate is expected to increase to about twice per month.

In the past two decades several civilian commercial uses of the space environment have been explored, in both the public and private sectors, and have reached varying degrees of maturity as demonstrations, operational systems or successful commercial ventures. These include the use of space systems for communication, navigation and the observation of the earth and its weather. These applications have achieved a sufficient degree of maturity so that the market for transportation to deliver satellites to orbit to perform these services is relatively well understood.

The use of the space environment for the processing of biological materials was suggested in the 1960s and the first experiment involving the electrokinetic separation of biological materials in space took place in 1971. In the early 1970s the manned space flights that provided the opportunities for space bioprocessing experiments occurred at roughly one year intervals in the Apollo, Skylab and Apollo-Soyuz missions. The electrokinetic separation experiments that were conducted in those early flights were generally encouraging but not conclusive in terms of the improved performance of these separation techniques in the space environment. In the main the interpretation of these early experiments was hampered by test equipment, instrumentation and procedural problems. Each successive experiment appears to have overcome most (if not all) of the problems encountered in the preceeding flights. However, progress was slowed by the infrequent flight schedule. In the period following the last of the early flights, the Apollo-Soyuz mission in 1975, both NASA and MDAC invested resources in

improving the reliability and performance of the electrokinetic separation equipment that would later fly in the Shuttle, and in improving the theoretical understanding of the behavior of electronkinetic separation processes in the zero-G environment. As a result of this investment, and as a result of the fact that the increased flight frequency of the Shuttle provides the opportunity to more rapidly correct problems as they are encountered in filght experiments, the performance of the equipment used in the Shuttle bioprocessing experiments has improved, and both the quality and quantity of results increased. Although much progress has been made since the first space-based electrophoresis experiment in the Apollo 14 flight in 1971, the use of the space environment for the processing of biological and pharmaceutical materials has not matured as rapidly as other applications. As a result, there is a great deal of uncertainty concerning the potential requirements of the biological and pharmaceutical industries for the use of the space environment. This uncertainty has made it difficult for NASA to plan for the space transportation needs of these industries and to develop a marketing strategy for the space bioprocessing area. The purposes of the study are to obtain a better understanding of the needs of the biotechnology and pharmaceutical industries for the use of the space environment, and to identify steps that might be taken by NASA to make the use of the space environment more attractive to these industries.

3. THE CAPABILITIES OF NASA TO SUPPORT THE PROCESSING OF BIOLOGICAL AND PHARMACEUTICAL MATERIALS

A wide variety of separation technologies have been developed and are used by the biotechnology and pharmaceutical industries. The ability to separate a biological substance of particular interest from impurities and/or other substances is an important step in the research, development and production of a new biological product. For example, during the research phase it is necessary to obtain small quantities of the biological substance of interest for analytical purposes. Quantities in the range of micrograms to milligrams are needed in the research phase. At this early stage cost is not a major factor and various separative techniques are often used in the laboratory to obtain the small quantities needed for analytical purposes. Further development of the substance, including testing and evaluation, requires quantities in the range of tens to hundreds of liters. During the development phase cost becomes increasingly important along with issues of the feasibility of production. Economic factors continue to be of major importance when the substance moves into the production phase. While electrokinetic separation techniques may be used to produce analytical quantities, in a unit-g environment electrokinetic separation techniques are not generally considered to be an economically feasible way of manufacturing the quantities needed for either research or production because of the limitations on throughput resulting from the effects of gravity.

While the emphasis of the space bioprocessing program to date has been on the research, development and demonstration of electrokinetic separative techniques in the zero-g environment, continued research may lead to other possible applications. For example, the characterization of the structure of proteins is important to the biotechnology industry. At the present time the characterization

of crystals and x-ray crystalography is limited by the fact that only a small number of proteins can be grown into crystals that are large enough for this purpose. Research with chemical substances has shown that larger crystals can be grown in zero-g than in a unit-g environment. A protein crystal growth experiment flown in the Shuttle/Spacelab 1 in November 1983 could lead to further research and development in the field of protein crystal growth in the space environment.[40,41]

3.1 What Does the Space Environment Offer?

Three environmental attributes: namely, gravity, atmospheric pressure and radiation are significantly different in space than on the surface of the earth. The differences in these attributes are the factors that cause physical processes such as electrokinetic separation or protein crystal growth to yield different results in space than on the surface of the earth. Table 3.1 summarizes the effects of these attributes on electrokinetic separation processes. The attribute of principal interest is the microgravity environment of space, and the resultant absence of gravity-induced effects in electrokinetic separation processes. While benefits to other processes from the hard vacuum and radiation environments of space may be

TABLE 3.1 ATTRIBUTES OF THE SPACE ENVIRONMENT AND THEIR RELATIONSHIP TO ELECTROKINETIC SEPARATION PROCESSES

ENVIRONMENTAL ATTRIBUTE	EFFECT OF INTEREST	SEPARATION PROCESS SPECIFIC EFFECTS	END EFFECT	COMMENTS
MICROGRAVITY	ABSENCE OF GRAVITY-INDUCED EFFECTS	REDUCES OR ELIMINATES SEDIMENTATION AND CONVECTION EFFECTS	IMPROVED THROUGHPUT AND PURITY	CAN BE ACHIEVED ON OR NEAR EARTH FOR SECONDS TO MINUTES, IN ORBIT FOR DAYS TO MONTHS
HARD VACUUM	CLEAN ENVIRONMENT	REDUCES POSSIBILITIES OF CONTAMINATION	IMPROVED PURITY	CAN BE ACHIEVED ON EARTH-BASED FACILITIES, BUT CAN BE ACHIEVED IN CONJUNCTION WITH MICROGRAVITY ONLY IN SPACE
RADIATION	ELECTROMAGNETIC AND PARTICULATE RADIATION	—	—	NO USE FOR THIS ENVIRONMENTAL ATTRIBUTE HAS BEEN SUGGESTED IN CONNECTION WITH SEPARATIVE PROCESSES

found through further research, the result of more then ten years of experimentation have clearly shown the benefit of the microgravity environment in terms of improved throughtput and the potential for improved resolution in electrophoretic, isotachophoretic and isoelectric separative processes.

3.2 NASA Capabilities for Microgravity Research and Development

NASA has a number of facilities and systems that are capable of simulating or providing access to the near zero-g environment of space. These can be broadly categorized into ground- and space-based facilities, where the ground-based facilities can simulate or provide access to the near zero-g environment for durations in the range of seconds to minutes, while the space-based facilities can provide exposure durations in the range of days to months.

3.2.1 Ground-Based Facilities

Table 3.2 summarizes the NASA ground-based (non-orbital) facilities. These consist of a drop tower, drop tubes, aircraft and sounding rockets.

The drop tower and drop tubes are located at the Marshall Space Flight Center, Huntsville, AL. The drop tower and drop tubes can achieve low gravity for

TABLE 3.2 NASA GROUND-BASED FACILITIES

FACILITY	LOCATION	DURATION OF EXPOSURE TO NEAR ZERO-G
DROP TOWERS	MARSHALL SPACE FLIGHT CENTER, AL LEWIS RESEARCH CENTER, OH	2 - 5 SEC.
DROP TUBES	MARSHALL SPACE FLIGHT CENTER, AL	5 SEC.
AIRCRAFT • KC-135 • F-104	JOHNSON SPACE CENTER, TX. DRYDEN RESEARCH CENTER, CA	20 - 25 SEC. 60 SEC. (REPEATED SEVERAL TIMES PER FLIGHT)
SOUNDING ROCKETS	WHITE SANDS, NM	5 MIN.

about two to five seconds in free fall. One of the drop tubes can use a melting apparatus in a bell jar. The bell jar and tube can be evacuated to low pressure or can be back-filled with helium. The melting apparatus can achieve temperatures in the range of 600 C to 3500 C and can accommodate samples in the size range of 1mm to 5mm. Both a 30m and 100m drop tube are availalbe. The drop tower is 100m high and can attain a free fall duration of about five seconds. The drop tower can accommodate an experiment payload of about 2' x 2.5' x 4'.

The sounding rockets are launched from the U.S. Army missile test range in White Sands, NM. NASA plans to call for launches twice per year; however, because of funding limitations there was only one launch (SPAR 9) in 1982, and one (SPAR 10) in 1983. The trajectory of the rocket creates a near zero-g condition in the vicinity of apogee for about five minutes. The rockets are capable of carrying a payload of about 1000 pounds in a payload compartment that is 16 inches in diameter and four feet high.

NASA also uses two aircraft to simulate the zero-g attribute of the space environment. The aircraft simulate the near zero-g attribute of the space environment by flying a parabolic trajectory. While each trajectory is brief, the maneuver can be repeated several times per flight. One is a KC-135 (a military version of the Boeing 707) based at Johnson Space Center in Houston, TX. The KC-135 can achieve near zero-g for about 25 seconds and is capable of flying this maneuver up to 50 times per flight. As it is basically a cargo aircraft, it can accommodate large payloads in a cargo bay that is 6' x 10' x 7'. The equipment can be attended by operators. The second is a modified military fighter aircraft, an F-104, based at Dryden Research Center, CA. Because of its capability to reach higher altitude, the F-104 can fly a parabolic trajectory for about 60 seconds. The maximum weight of experiments that can be used in the F-104 is 70 pounds.

Because electrokinetic separation processes require process times that are longer than the maximum duration of near zero-g exposure that can be achieved in the NASA ground-based facilities, the ground-based facilities have not been used for bioprocessing research involving electrokinetic separation.

3.2.2 Space-Based Facilities

Although the space bioprocessing experiments that have flown to date are not either unusually large or heavy, they have not been automated and all have required some degree of human intervention. As a result, all of the bioprocessing experiments have flown in manned spacecraft. For this reason, the Space Shuttle is the space-based capability that will be used for the next several years to support space bioprocessing research and development. With its high flight frequency of about once per month in 1984, building to about twice per month in a few years, and its ability to carry mission specialists to attend to the experimental equipment, the Shuttle has and will continue to be used for space bioprocessing work both by NASA and the private sector.

As shown in Table 3.3, the Shuttle provides a wide range of accommodations for materials processing experiments in the space environment. These range from small self-contained experiments that operate in an automated manner, and interface with the Shuttle only for power and operating mode commands, to large, complex experiments that are installed in the Shuttle payload bay and are operated by a member of the Shuttle flight crew working for the organization conducting the experiment. For example, the MDAC continuous flow electrophoresis device has been accommodated in a mid-deck locker in the crew compartment area, while the protein crystal growth experiment was performed in the Spacelab. The Spacelab is a habitable, pressurized module that is 9' long by 13' in diameter. The Spacelab system is modular and can be configured as one or two habitable modules in

TABLE 3.3 NASA SPACE-BASED CAPABILITIES

PROGRAM	STATUS	CONTACT	COMMENTS	DURATION OF EXPOSURE TO NEAR ZERO-G
SMALL SELF-CONTAINED EXPERIMENTS	ACTIVE	DONNA MILLER NASA HEADQUARTERS WASHINGTON, DC	SEVERAL EXPERIMENTS HAVE FLOWN. POLICY IN PLACE.	10 DAYS
CAPACITY FOR OPPORTUNITY PAYLOAD EXPERIMENTS • MULTI-POSITIONARY EXPERIMENT SUPPORT STRUCTURE (MPESS) • COMMERCIAL SYSTEMS	PLANNING	JOHN HOYE ROBERT LOHMAN NASA HEADQUARTERS WASHINGTON, DC	CONCEPT IS IN DISCUSSION. POLICY FOR ACCESSING DOES NOT EXIST.	10 DAYS
SPACELAB • PALLETS • HABITABLE MODULES	ACTIVE	MICHAEL SANDER NASA HEADQUARTERS WASHINGTON, DC	FIRST FLIGHT STS-9. POLICY FOR COMMERCIAL USE NOT YET APPROVED.	10 DAYS
CREW COMPARTMENT AREAS (SHUTTLE)	ACTIVE	RONALD PHILIPS NASA HEADQUARTERS WASHINGTON, DC	MID-DECK USED BY MDAC/J&J. POLICY FOR COMMERCIAL USE NOT ESTABLISHED.	10 DAYS
PAYLOAD BAY (15 FT. DIA. X 60 FT. LONG) (SHUTTLE)	ACTIVE	CHESTER LEE CUSTOMER SERVICES NASA HEADQUARTERS WASHINGTON, DC	ESTABLISHED POLICY FOR COMMERCIAL USE. MINIMUM BUY IS 1/4 OF PAYLOAD BAY.	10 DAYS
SHUTTLE LAUNCHED SPACECRAFT (UP TO 65,000 LBS.)	ACTIVE	CHESTER LEE CUSTOMER SERVICES NASA HEADQUARTERS WASHINGTON, DC	LAUNCH CAPABILITY DEMONSTRATED. REVISIT CAPABILITY TO BE DEMONSTRATED IN STS-13	6 TO 9 MONTHS

combination with pallets that are neither habitable nor pressurized. Spacelab can accommodate up to about 6000 pounds of evenly loaded equipment. The experiments are rack mounted, and those installed in the modules can be accessed during flight. The experiments can be self-contained, or can be controlled from the Spacelab module, the Shuttle aft deck, or the ground.

With its present capability the Shuttle can provide up to ten days of exposure to the near zero-g environment. This limitation on on-orbit duration is probably the only performance constraint on the use of the Shuttle for space bioprocessing. Although proposals have been made to extend the on-orbit duration capability of the Shuttle, at the present time the only way to obtain a longer exposure to near zero-g environment is to use the Shuttle to place an automated spacecraft into orbit. With its revisit capability the Shuttle could support space bioprocessing

work by revisiting the automated spacecraft for maintenance and to replenish its supply of expendables and raw materials, and to return the processed product to earth. The Shuttle launched automated spacecraft could then remain in orbit and be revisited at several month intervals by the Shuttle.

Example schedules for the use of the Shuttle are shown in Figure 3.1. These schedules are compatible with the times needed for the development of flight experiment equipment and the planning for flight experiments. For example, small self-contained payloads require a lead time of about 18 months and should be at the launch site about two to six months before the scheduled launch for integration with the Shuttle. Larger payloads such as those installed in the payload bay need longer lead times for development and integration. Equipment with complex interface and design requirements may require a lead time of up to three years. Once installed in the Shuttle, access to the experiment or payload can be attained up to a few hours before launch. These schedules are typical, and NASA has shown that it can be flexible to accommodate the schedule needs of precommercial and commercial payloads.

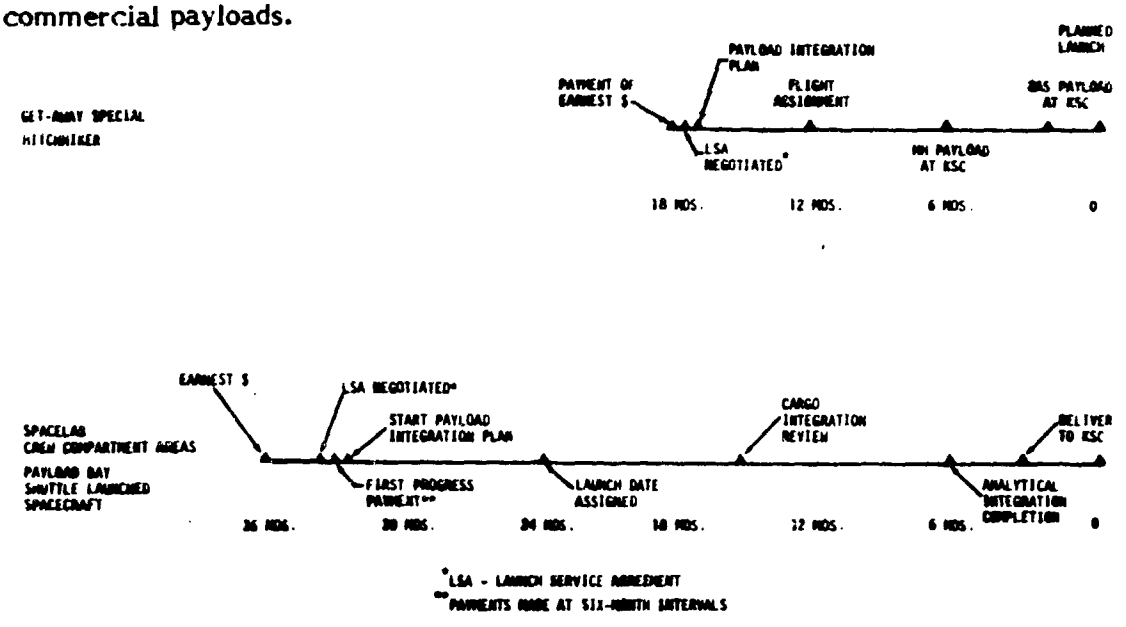

FIGURE 3.1 EXAMPLE TIMELINES FOR ORBITAL FACILITIES

In January 1984, President Reagan proposed that NASA begin the development of a space station that would provide the capability for a permanent manned presence in space. Space bioprocessing is one of the commercial applications that has been suggested for the space station. Because of the lead times for development and production, it is not likely that the first U.S. space station will be operational before the early 1990's. For this reason, the Shuttle, and its capability to deliver, retrieve and revisit payloads will remain as the principal space-based capability to support bioprocessing for the next eight to ten years.

3.3 NASA/Industry Working Relationships

Under the Space Act of 1958 that created NASA, the agency is mandated by Congress to conduct its activities in a manner that contributes to the preservation of the role of the U.S. as a leader in aeronautical and space science and technology and their applications. As the technology and systems developed by NASA began to mature the agency recognized that certain of these had commercial potential, and it began an on-going effort to find the mechanism to involve the private sector in the commercialization of these technologies and systems. In the case of space bioprocessing, this involved a clear recognition on the part of NASA that it was responsible for the development of the technology base that could lead to private sector ventures, but that it had no direct involvement in the processing of materials for commercial markets. The development of specific commercial products and/or services from the NASA technology base and capabilities was and continues to be regarded as the sole domain of the private sector.

In the late 1970s, NASA put in place institutional and contractual arrangements to foster the participation of the private sector in space bioprocessing and other areas of space materials processing.[42] The institutional arrangement took the form of establishing a Commercial Applications Office in the Materials

Processing in Space Projects Office in the Marshall Space Flight Center. This office was assigned the responsibility of assisting prospective commercial interests by providing information on NASA sponsored work, and by providing access to the work and to NASA capabilities. The office was also charged with the job of clarifying the policies of NASA with regards to commercial rights in intellectual property, liabilities, equipment leasing and pricing. In August, 1979, Dr. Robert A. Frosch, then the administrator of NASA, took a major step to involve NASA in a more direct way in the process of commercialization when he issued NASA Notice 79-70, Guidelines Regarding Joint Endeavors with U.S. Domestic Concerns in Materials Processing in Space. These guidelines recognized that the normal market forces had not brought about the participation of the private sector, and that it was necessary for NASA to encourage the entry of the private sector into space materials processing through the sharing of cost and risk. The guidelines defined a new concept for the public sector called a Joint Endeavor. Under the Joint Endeavor concept the private sector could propose to enter into a formal agreement with NASA for precommercial research and development in space materials processing for work that was both consistent with NASA program objectives, and which involved a significant level of technical uncertainty and risk. If the proposed private sector activity met NASA's criteria, NASA could provide flight time on the Shuttle, technical support and the use of other facilities at no cost to the commercial participants. A fundamental ground rule of the Joint Endeavor concept is that each party funds its own participation. In January 1980 MDAC entered into a Joint Endeavor Agreement with NASA for research, development, flight experimentation and precommercial demonstration of the practicality of the use of continuous flow electrophoresis technology for space materials processing.[43] Under the terms of this agreement, NASA will provide

MDAC with a number of flights of the MDAC continuous flow electrophoresis equipment in the Shuttle at no cost to MDAC. Further, NASA agreed not to enter into other Joint Endeavor Agreements to provide access to the Shuttle at no cost to other commercial or international entities engaged in the development and demonstration of electrophoretic separation technology for the six years of the agreement. In return, MDAC agreed to provide the continuous flow electrophoresis apparatus, test samples and to actively pursue the commercial potential of this separative technology and the resultant products. At a later date the Ortho Division of J&J became associated with MDAC in the exploration of the commercial products that might be obtained in this space bioprocessing venture.

Since 1980, the concept of the Joint Endeavor Agreement has been expanded to provide for other forms of working relationships between industry and NASA. Figure 3.2 illustrates this range of possible working relationships. With the addition of Guest Investigator and Technical Exchange Agreements, NASA now has

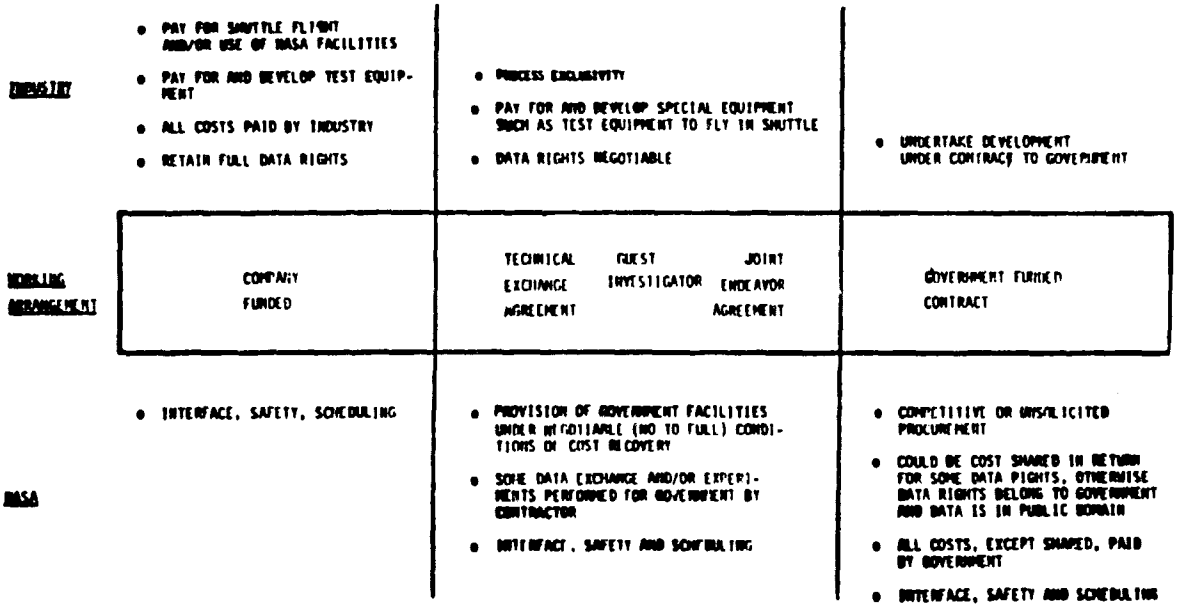

FIGURE 3.2 THE RANGE OF NASA/INDUSTRY

a continuum of possible flexible and cooperative working relationships with the industry. In Figure 3.2 the left and right hand zones depict the more conventional forms of working relationships between government and industry, while the center zone illustrates the cooperative, risk sharing relationships. In the Company Funded mode (left), all costs are borne by industry, with NASA retaining responsibility for interface control, safety and scheduling. The objectives are selected by industry and all data rights are retained by industry. In the Government Funded Contract mode, NASA can contract with industry (or a university) to perform the work and all costs are borne by the government. Variations of the Government Funded Contract mode include degrees of cost sharing, but in general, the objectives are selected by the government and data rights are the property of the government. The cooperative modes imply a degree of mutual interest between industry and NASA, with a progression of involvement and commitment from an agreement to exchange data, to the possibility of industry appointing a scientist to collaborate with a NASA sponsored investigator to a Joint Endeavor Agreement to share cost and risk. In each of these three cooperative modes the government does not fund any of the work done by industry, nor (under the terms of the agreement) does industry compensate NASA for data or services. Each party funds its own activities separately, working together toward the common objective of commercializing the NASA developed space materials processing technology. With this continuum of working relationships NASA and industry can design a relationship to fit the mutual needs of both parties. Through these cooperative agreements industry and government can achieve mutually supportive roles in space bioprocessing experimentation and development.

4. PERCEPTIONS OF U.S. BIOTECHNOLOGY AND PHARMACEUTICAL COMPANIES CONCERNING THE USE OF THE SPACE ENVIRONMENT

At the outset it was decided to focus this study on a particular application of NASA capabilities; namely, space material processing. Within this broad context, it was then decided to examine the potential uses of the space environment by the biotechnology and pharmaceutical industries. These choices were based upon the fact that NASA has been involved in research, development and experimentation with biological materials in the space environment for nearly 15 years, and the desire to focus this work upon a specific industrial application.

An important objective of this study was to assess the needs and attitudes of U.S. biotechnology and pharmaceutical companies concerning the potential use of the space environment. The insights gained from an improved understanding of the needs and attitudes of these industries could then be used to identify actions that might be taken by NASA to facilitate the development of future commercial space bioprocessing ventures. Today, the Space Shuttle is the predominant image of the space program. Moreover, the Space Shuttle represents the likely NASA capability that will be used during the next decade to transport to orbit, revisit or retrieve space bioprocessing equipment. With the present capability of the Shuttle the space bioprocessing equipment can be attached to the Shuttle, remain in the near zero-g environment for up to ten days and then returned to earth, or the Shuttle can be used to deliver automated space bioprocessing spacecraft to orbit. These automated space bioprocessing laboratories could be revisited by the Shuttle at monthly or longer intervals to replenish consumable materials and bring back the finished product. Because of the predominance of this existing capability, the study of necessity focussed on the potential needs and perceptions of the industries relative to the Space Shuttle and systems that could be supported by the Shuttle.

In this manner, the primary objective dealt with issue of the potential use of the space environment by the biotechnology and pharmaceutical industries, and specifically with the potential of NASA as an agency, and the Space Shuttle as transportation system to support a broadening of commercial interests in space bioprocessing.

A second objective was to test the feasibility of a direct approach to the marketing of space transportation. In this context, the direct approach involves the identification and contact of potential "customers" by "sales" personnel in an effort to "sell" the use of the Space Shuttle. This view of a direct approach to marketing can be contrasted to an indirect approach which relies upon advertising (both paid and free) to stimulate potential customers to seek out NASA. Direct marketing is proactive while indirect marketing is largely reactive. Thus, the second objective dealt with the question of tools to support a direct marketing approach, and the success of this type of approach in eliciting interest on the part of potential customers.

4.1 Approach

To satisfy the objectives discussed above, an approach was developed that involved the use of a direct marketing approach to assess the perceptions of U.S. biotechnology and pharmaceutical companies concerning the use of the space environment for research and development that could lead to commercial space environment for the research and development that could lead to commercial space bioprocessing ventures. Figure 4.1 is an overview of the approach.

Based upon the objectives, the product to be examined in the market assessment was identified as the use of the space environment, and specifically the use of the Space Shuttle to provide the access to the space environment. The potential customers for the use of the space environment were identified as U.S.

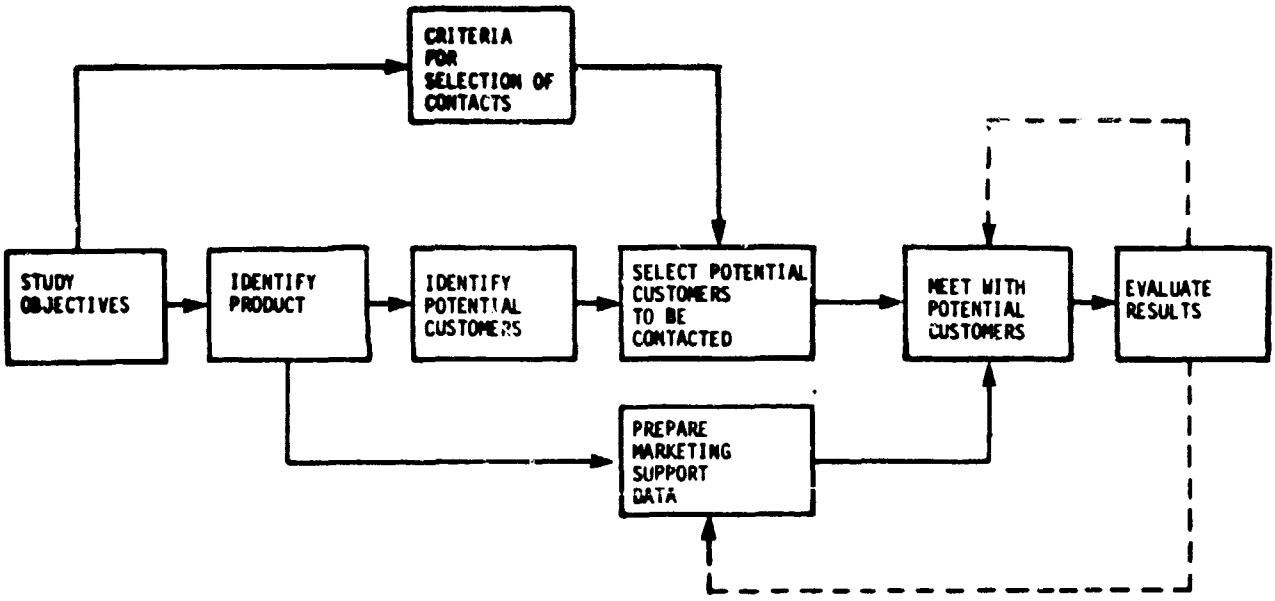

FIGURE 4.1 OVERVIEW OF APPROACH USED IN ASSESSMENT

companies involved in biotechnology and/or pharmaceutical research, development or product manufacturing. As shown in Figure 4.2, criteria were developed for the selection of the companies to be contacted. Using standard industry and business studies a candidate list of nearly 100 biotechnology and pharmaceutical companies was prepared. The list was reviewed with representatives of the Industrial Biotechnology Association (IBA) and the Pharmaceutical Manufacturers Association (PMA) to identify those companies that were considered by their peers to be more innovative and forward looking in their research programs. The objectives of the study were reviewed with the IBA and PMA and the cooperation of these two trade associations were solicited. The trade associations assisted by identifying specific individuals in their member companies that they believed would be the most productive point of initial contact. The value of this assistance cannot be overstated, particularly in dealing with the large pharmaceutical companies that have large headquarters staffs and multiple divisions. Through the assistance of

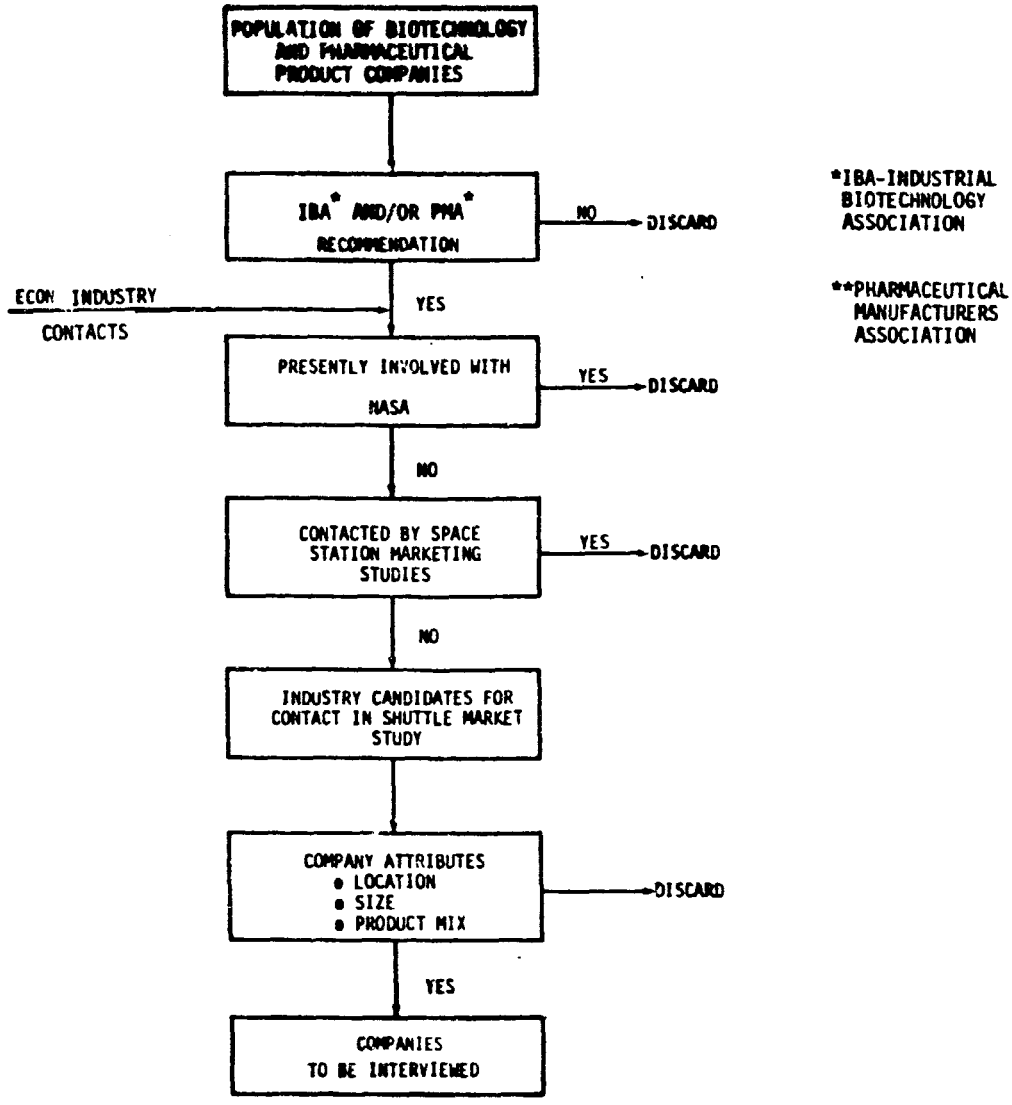

FIGURE 4.2 SELECTION CRITERIA FOR COMPANIES TO BE CONTACTED

these industry associations the study team was able to identify the individual who was most likely to be interested or receptive to the proposal for a meeting to discuss the potential use of the space environment.

Those companies in which the ECON study team had contacts as a result of previous work with this industry were also identified. In order to remove potential bias from the set of companies to be contacted relative to the feasibility of the

direct marketing approach, those companies presently involved with NASA either through a Joint Endeavor Agreement (JEA) or through the space station studies were removed from the list. The remaining list was further narrowed on the basis of product mix, and those companies located in Canada and Europe were removed from the list. The remaining list contained 19 companies, and was roughly evenly divided between large, traditional pharmaceutical companies and newer biotechnology companies.

The 19 companies that were contacted are listed in Table 4.1 along with the result of the contact process. The contact process was started by a letter to a senior person, usually a Vice-President in the case of the large pharmaceutical companies, or the President in the case of the biotechnology companies. The ability to make an initial contact at a high level was believed to be important at the outset of the study, as experience of the study team in similar research projects had shown that there is a greater likelihood of the data collection process succeeding if it has the attention of top management. Appendix A is a copy of this letter. Telephone calls were then made to set up the meeting. As shown in Table 4.1, ten of the 19 contacts resulted in either a statement that the company was not interested in participating in the meeting, or in no response. The no response and not interested category is almost evenly divided between large pharmaceutical companies and smaller biotechnology companies so that it is difficult to draw any conclusion concerning the relationship between interest and size of company. Of the nine companies with which meetings were held, four were biotechnology companies, four were large pharmaceutical companies and one was a start-up venture in separative technology in the biotechnology field.

In parallel with the contact process, the material to be used in the meetings with the companies was prepared. The material consisted of a presentation style

TABLE 4.1 BIOTECHNOLOGY AND PHARMACEUTICAL COMPANIES CONTACTED

NAME	ADDRESS	RESPONSE
Amgen	1893 Oak Terrace Lane Newbury Park, CA 91320	None
Biogen	14 Cambridge Center Cambridge, MA 02142	MEETING
Biotech International	85 Bolton Street Cambridge, MA 02140	MEETING
Cetus Corp.	1400 53rd Street Emeryville, CA 94608	None
Ciba-Geigy	556 Morris Avenue Summit, NJ 07901	None
Collaborative Research	128 Spring Street Lexington, MA 02173	None
Damon Biotech	115 Fourth Avenue Needham Heights, MA	MEETING
Genetics Institute	225 Longwood Avenue Boston, MA 02115	Not Interested
Genex Corp.	6110 Executive Blvd. Rockville, MD 20852	MEETING
GIBCO/BRL Laboratories	8717 Government Circle Gaithersburg, MD 20877	Not Interested
Merck, Sharp & Dohme	PO Box 207 Rahway, NJ 07065	MEETING
Pharmacia	800 Centennial Avenue Piscataway, NJ 08854	None
Pfizer, Inc.	235 E 42nd Street New York, NY 10017	Not Interested
Sandoz, Inc.	Route 10 E. Hanover, NJ 07936	Not Interested
Sepracor	1101 State Road Princeton, NJ 08540	MEETING
Shering-Plough Corp.	60 Orange Street Bloomfield, NJ 07003	Not Interested
Smith-Kline-French	1500 Spring Garden Street Philadelphia, PA 19101	MEETING
Squibb	Princeton, NJ 08540	MEETING
The Upjohn Co.	7000 Portage Road Kalamazoo, MI 49001	MEETING

report titled "The Potential Use of the Space Environment for the Processing of Biological Materials." The presentation was designed to be covered in about one hour and was intended to facilitate discussion. It introduced the topic, reviewed past and current flight experiments, and provided an overview of NASA capabilities to support bioprocessing research in a microgravity environment. The presentation

report is contained in Appendix B. Following the first meeting a few deficiencies in the presentation report became apparent. The report was modified and the style of the meeting was changed slightly from a formal presentation to an informal discussion with the report as the focus.

4.2 Structure of the Meetings

The meetings with the participating companies were intended to follow the format of informal discussions to the maximum extent possible, rather than the format of a presentation or a structured interview. In the meetings an effort was made to begin a dialogue with the representatives of the participating company, and to place the emphasis of the discussion on those aspects of the past or present space bioprocessing experiments, on those aspects of NASA's capabilities, or on those aspects of the possible cooperative working arrangements between NASA and industry that were of most interest to the company. However, the meetings did have specific information gathering objectives as well as information transfer objectives. As discussed in Section 4.1, the information transfer objectives were achieved through the discussion of the material contained in Appendix B. Figure 4.3 illustrates the general flow and structure of the meetings. The decision structure shown was adhered to to the maximum extent possible without disrupting the focus of the industry participants on specific aspects of the NASA program that might be of interest to them. In some cases, at the conclusion of the meeting it was possible to address questions that had not been previously answered in a summary of the discussion. However, as will be discussed below, all of the questions were not covered in all of the meetings.

4.3 Responses

Since meetings were held with only nine companies it is not meaningful to view the results as a database that is amenable to statistical analysis. With this

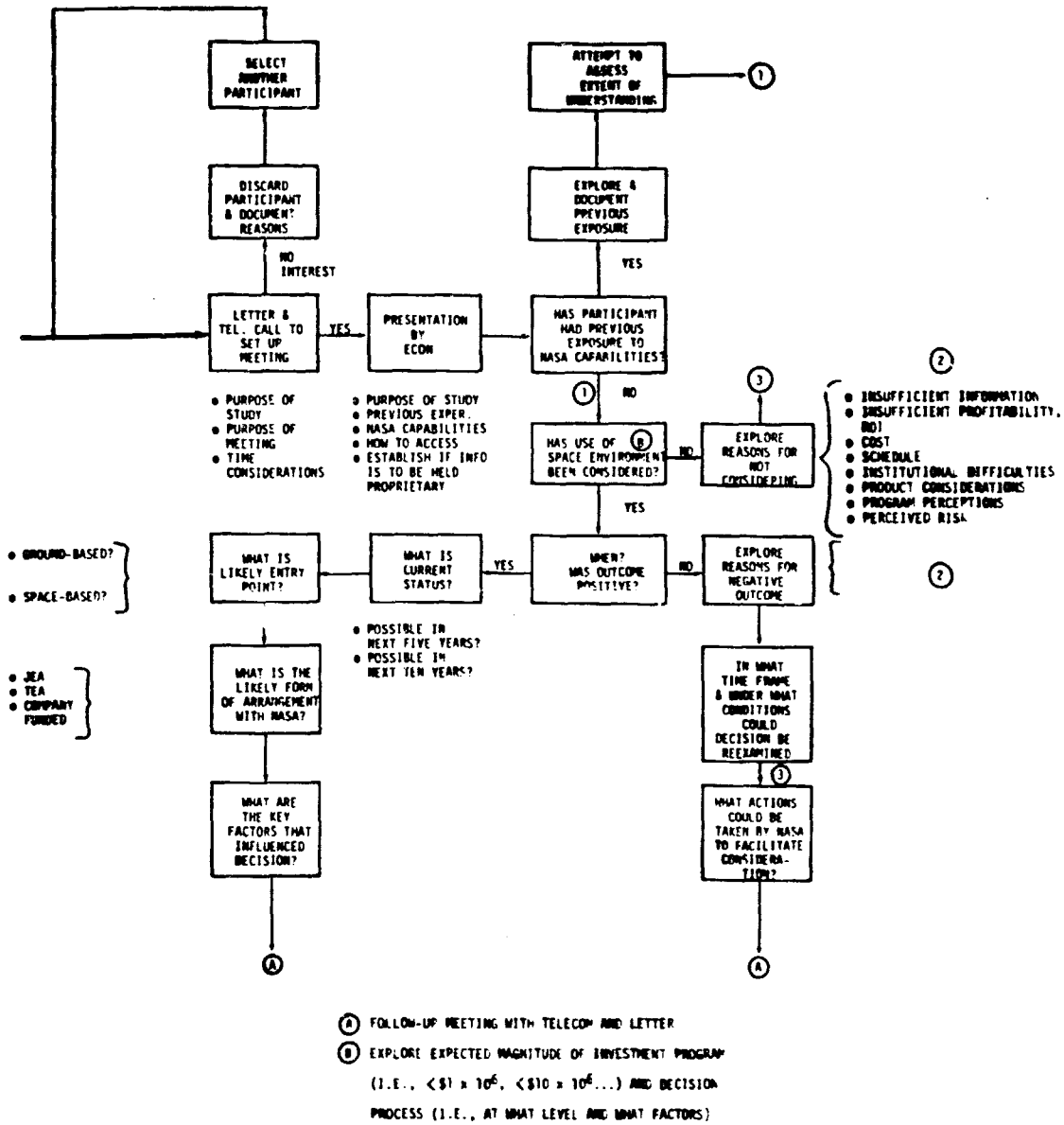

FIGURE 4.3 INFORMATION OBJECTIVES FOR MEETINGS WITH INDUSTRY

number of participants it is more appropriate to look for general trends and positions articulated in discussion that might be indicative of the perceptions of these industries concerning the NASA program and the opportunities for commercial development. Several general observations of this nature can be made from the meetings, and they are discussed in the following sections. The detailed reports of the meetings with the individual companies are contained in Appendix C.

4.3.1 Interest in Space Bioprocessing

Nineteen companies were contacted by letter and telephone with the specific objective of setting up a meeting. Only five companies responded negatively with a statement that they were not interested in participating in the study. Nine companies expressed an interest in participating and meetings were held with these nine companies. In five additional cases it was not possible to reach the individual to whom the letter had been addressed, or to get that person to designate an alternate contact. It should be noted that only about one month elapsed between the start of the contact by letter and the meetings with the participating companies. With additional time and persistence it is likely that it would have been possible to arrange interviews with some of the five companies where contact could not be made in the time available for this study.

The interest of these industries in space bioprocessing was also evident in the meetings. All of the companies that participated asked for additional information and/or follow up meetings. In general, the requests were aimed at obtaining information about a specific area of experimentation, to obtain information that would be useful to the company in their consideration of the use of the space environment, or to more widely disseminate the information discussed in our meeting.

4.3.2 Availability of Information

Although space bioprocessing is not a new field, and the potential benefits have been widely publicized, a disconcerting result of the meetings was the lack of prior knowledge of the NASA program on the part of the industry participants. Most of the participants were generally aware of the fact that NASA was involved in space bioprocessing research and development, and that MDAC had flown experiments on the Shuttle. Few had specific knowledge of the separative

experiments conducted by NASA or MDAC. Similarly, few of the participants were aware of the opportunities for cooperative pre-commercial research and development programs (such as the JEA) with NASA. The most common answer to questions aimed at probing how the participants maintained their knowledge of the space bioprocessing program was through the local TV and newspapers. One of the participants said that his company reviewed the NASA testimony to Congress, or had given testimony in support of the NASA space materials processing program and two said that they used personal contacts within NASA to obtain information.

4.3.3 Have the Companies Considered the Use of the Space Environment?

Of the nine companies that participated in this study, three had previously considered the possible use of the space environment. In each case the consideration was informal and did not reach the status of a formal proposal within the company before it was discarded. In the case of a start-up biotechnology company the proposal was set aside because of a lack of resources, while two large pharmaceutical companies indicated that economics was a major factor in their negative decision. None of the companies apparently took the step of discussing their preliminary concept or proposal with NASA. A lack of information was the most usual reason given for not considering the possibility of conducting space based biotechnology or pharmaceutical research.

4.3.4 Electrokinetic Separation as the Focus of Research in Space Bioprocessing

Several of the companies that participated in the study questioned the reasons for the focus of the NASA and MDAC space bioprocessing work on electrokinetic separative techniques. In particular, two of the biotechnology companies and one of the pharmaceutical companies essentially characterized the continuous flow electrophoresis work in space as a "solution looking for a problem." The fact that electrokinetic separation techniques are hampered by sedimentation

and convection effects in a unit-g environment was not questioned, and it was agreed that the absence of gravity in space could improve the performance of these separative processes. However, it was pointed out that the problems resulting from the effects of the unit-g environment on electrokinetic separation were recognized more than a decade ago. As a result, techniques such as gel electrophoresis have been developed to reduce the effects of gravity in electrokinetic separation proceesses, and that other separative processes such as affinity chromotography that are not affected by gravity have since been developed.

Several of the participants suggested that research in the field of protein crystal growth in the space environment might be a productive area to investigate. Others suggested the investigation of effects of the absence of gravity on cell efficiency (productivity and fusion frequency), magnetic separation and the behavior of immobilized enzymes.

4.3.5 The Economics of Operating in Space

There was a widespread perception amongst the participants that the cost of operating in space was prohibitively high, and that economics would probably preclude the use of the space environment for the manufacturing of production quantities of biological or pharmaceutical materials. Production quantities were generally identified to be in the range of hundreds to thousands of kilograms. The perceived economic barrier to production in turn becomes a barrier to the consideration of the space environment for product development (i.e., the manufacture of preparative quantities), as cost and the considerations of scale-up to production become important in the development phase. For example, one of the participating companies said that they had just built a production facility that would hopefully have a life of about forty years at a cost of about one Shuttle flight (about $70 million). In other cases a concern was expressed that the

company lacked the technical capability to develop the test equipment to work in the space environment, and that the company would have to bear the entire cost of developing the space test facility. As indicated in Section 4.3.2, most of the companies were unaware of the opportunities for a cooperative research and development program with NASA, and were certainly not aware of the possibility for cost-sharing through cooperative programs. This is a clear challenge to NASA to show the cost effectiveness of space processing for both research and development, and production.

4.3.6 Participant Reaction to a Direct Marketing Approach

A major concern at the outset of this study was the question of how the participants would react to a direct marketing approach. The concerns ranged from the accessibility of the key industry personnel contacted for the proposed meetings, to the possibility of negative reactions on the part of the participants to the use of the presentation style report as a means of transferring information about the NASA program to the participants and focussing the resultant discussion. It is clear from the results of this study that there is sufficient interest in the biotechnology and pharmaceutical companies in the space program, the Space Shuttle and space bioprocessing to motivate key industry personnel to make themselves available for the type of meeting conducted in this study at their facility. Furthermore, in eight out of the nine meetings the presentation style report worked well as a means of conveying information and eliciting and focusing discussion. In the ninth case the principal industry representative was available for only one hour, and it was not possible to cover the presentation material and allow for a discussion in the alloted time. As a result, only parts of the presentation material were covered in this meeting.

4.4 Interpretation of Responses

4.4.1 The Need for a Continuing Dialogue and for Additional Information

All of the companies contacted in this study indicated a desire to continue to interact with NASA on the subject of the opportunities for commercial participation in the space bioprocessing program. This request took several forms. Several of the companies asked if it would be possible to arrange follow-up meetings with NASA personnel involved in scientific aspects of the NASA program. One major pharmaceutical company specifically asked if it would be possible to provide an individual with a broad scientific background in space bioprocessing to talk to their senior scientific people. The same pharmaceutical company expressed an interest in having a NASA person discuss the engineering aspects of space bioprocessing with a large group of their middle management people. One of the biotechnology companies stated that they would be interested in convening a special meeting of their scientific board, consisting or top level research scientists from Harvard and MIT for a further discussion of the scientific aspects of the program.

The same companies asked for additional information in several forms. The most common request was for databases that their staff could examine at their convenience or when a particular requirement arose in the conduct of their own work. For example, almost all of the participants asked if NASA could provide information such as titles, abstracts and Principal Investigator identification on the space bioprocessing program. They asked for information on the nearly 400 completed or planned Get-Away-Special experiments and on the equipment and facilities for space experimentation that are available from NASA. It is clear from the comments of the industrial participants that databases of the sort described could be a very useful tool in future interaction with the biotechnology and pharmaceutical industries.

4.4.2 The Need to Demonstrate the Potential Usefulness of the Space Environment to Multiple Aspects of Space Bioprocessing Research

Several of the participants, particularly biotechnology companies, questioned the emphasis of the NASA program on separative research. Comments such as "outdated technology," "solution looking for a problem" were made by several participants. One participant went so far as to state that while the pharmaceutical industry viewed space bioprocessing (i.e., space-based electrokinetic separation research) as a means to an end (the end being a new chemical or biological entity), it appeared as if current programs were perceived by their sponsors as an end unto themselves. In this connection, several of the participants suggested that other areas of research such as the effect of zero-g on cell productivity and on protein crystal growth were also potentially important. Given these suggestions by the participants in the study, it would appear to be worthwhile for NASA to consider other avenues of research in order to avoid the equation of space bioprocessing with space-based research in separative techniques.

4.4.3 Economic Feasibility

Almost every discussion with the industry particpants in this study eventually got to the issue of cost and economic feasibility. Although the participants were receptive to concepts of low cost experiments such as the Get-Away-Special, or risk sharing for pre-commercial work through mechanisms such as the JEA, the participants were uneasy about the possible costs of processes that might require repetitive flights or production processes that might require space-based manufacturing facilities. One possible interpretation of this response is that industry does not have sufficient data or experience with which to formulate its own estimates of the economic feasibility of space-based research, development or production. While it would clearly not be desirable for NASA to put a price tag on an industry program that does not yet exist, it would be desirable for NASA to be in a position

to remove some of the uncertainty in the mind of the industry concerning cost. Whether this is best done by creating a few standard examples that might bracket the range of possible interest, or by creating a parametric cost/price model that might be used interactively and iteratively by NASA with industry personnel needs further consideration.

4.4.4 Direct Marketing Approach

The industry participants were receptive to the direct marketing approach used in this study. The 19 initial industry contacts made in this study resulted in nine highly productive meetings. With additional time and resources it is likely that the number of meetings could have been increased. The presentation style material that was prepared for these meetings, as shown in Appendix B, worked well to focus and generate discussion. Based on the reactions of the industry participants, it is believed that this type of material could be an important adjunct to future efforts by NASA to develop the use of the space environment by biotechnology and pharmaceutical companies.

5. ACTIONS THAT COULD BE TAKEN BY NASA TO FACILITATE THE MARKETING OF THE SPACE SHUTTLE TO THE BIOTECHNOLOGY AND PHARMACEUTICAL INDUSTRIES

The results of the study support several general conclusions concerning the perceptions of the industries that participated in this study relative to the potential use of the space environment for the processing of biological materials. The conclusions in turn can lead to recommendations for action that could be taken by NASA to facilitate the marketing of access to the space environment to these industries. These conclusions and recommendations are discussed in the following sections.

5.1 Improve the Quality and Quantity of Information Available to Industry

As discussed in Sections 4.3.1, 4.3.2 and 4.4.1, few of the industrial participants in this study had any specific information concerning the NASA space bioprocessing program. Similarly, the possibility of establishing risk-sharing cooperative arrangements between industry and NASA for space bioprocessing R&D was not understood by the industrial participants. Many of the companies asked for additional information. In some cases this took the form of a request for further visits by NASA personnel to meet with their top level management people on various aspects of the space bioprocessing program. Most often the request was made for additional data on completed or planned experiments, or data on the NASA owned equipment that might be available for use in cooperative experiments. Based upon this finding it is recommended that NASA develop and maintain several databases for use in supporting further marketing activity to these industries. For example, one database could cover all of the planned and/or contemplated space bioprocessing experiments and include information such as titles, abstracts, Principal Investigation identification and references. Another

1st let's respond to specific co. by co. requests - where's the list of these? Appendix C

database could include descriptive and performance information on space processing equipment that has been developed by NASA. In addition to the two databases mentioned above, a third database containing information on the Get Away Special experiments would be of help in responding to the type of requests for additional information that were raised in the meetings conducted in this study. These databases will prove useful to NASA customer representatives in responding to requests from industry concerning prior of planned experiments, and/or the availability of existing NASA equipment to support future industry experiments programs.

As an initial step in developing these databases, it is recommended that NASA conduct a comprehensive review and study of the availability of the information needed to support these databases. This should include an examination of the sources and nature of the data, the needs of NASA marketing personnel for the uses of the information, as well as the formats and alternative mechanizations for the databases.

In addition to the development of these databases to support future marketing efforts, it is recommended that NASA follow up the specific requests for additional information as noted in the individual industry meeting reports included in Appendix C of this report.

Longer term information transfer programs should also be considered. These might include a quarterly newsletter with a summary of the results of current programs and/or discussion of plans. The newsletter could also provide a convenient format for periodically restating the opportunities for cooperative programs. An annual conference or workshop specifically on the subject of space bioprocessing might also be a good method of information transfer. The conference might be hosted by a university under the auspices of NASA, or it might be

Get Dick McCormack to work Tech. Brief Comm'l Space Add
- Ck. w/
- Bob E
- Len A
- Azeez

held in conjunction with Industrial Biotechnology Association or Pharmaceutical Manufacturers Association meetings.

5.2 Remove Some of the Uncertainty Concerning the Cost of Operations in the Space Environment

As might be expected, the issue of the cost of operating a production facility in space came up in nearly every meeting. In some cases there was a tendency to discard the possibility of using the space environment for the manufacture of production quantities of biological or pharmaceutical materials because of the expectations of very high costs. In other discussions, concepts that might require repetitive flights were dismissed because of the expectation of high costs. With this perception, it is not likely that industry will consider the use of the space environment for R&D that could lead to a need for a space-based production facility or for repetitive flights. In nearly all of the contacts made in this study the industry participants had no real information concerning the cost of operating in the space environment. The perception of the high cost of space operation may be difficult to correct, as the costs most often given in the press for the use of the Shuttle are either the cost of the vehicles to the government or the cost to a customer for the occupancy of the full payload bay. It is not likely that the kinds of experiments suggested by the companies that participated in the study will lead to a need for the full payload bay.

At the time of this study pricing policies have been published for the Get Away Specials and the payload bay. Pricing policies have not been approved for commercial use of other payload areas likely to be used for bioprocessing experimentation, such as Spacelab and the Capacity for Opportunity Payloads. To clarify this situation it is recommended that NASA develop policies for commercial use of these other payload areas, and that pricing policies for these payload areas be published. As discussed in Sections 4.3.5 and 5.2, it is possible that the current

lack of information and the presence of a considerable quantity of misinformation is an inhibiting factor in consideration of the use of the space environment by industry. Moreover, as pointed out in Section 4.3.2, few of the industry participants were aware of the opportunities for cooperative programs that could reduce the cost of space-based research and development. To support future marketing, it is recommended that NASA develop a simple parametric cost/price model for the use of these other payload areas such as Spacelab and Capacity for Opportunity Payloads. This model, along with improved information on possible cooperative arrangements between industry and NASA, can then be used by NASA customer representatives to help industry develop a better perception of the true cost of using the Shuttle for space bioprocessing.

5.3 Marketing Strategy

The fact that direct contact with potential customers can be an important and productive part of a NASA marketing strategy to sell access to space and/or the use of the space environment to the biotechnology and pharmaceutical industries is reinforced by this study. However, it must be realized that the use of a particular marketing approach must be carefully integrated into an overall marketing strategy, and that what is deemed to be an appropriate strategy and approach today may need to be adjusted in the future to a changing perception of national needs and the marketplace. While it is clear that the industries contacted in this study are receptive to a direct marketing approach, this does not imply that direct marketing should be used to the exclusion of all other marketing mechanisms. In fact, one of the findings of this study is the need by the industries contacted for additional information. Other mechanisms such as publications, seminars, presentations of scientific results at meetings are necessary to support a direct marketing approach. Follow-up with potential customers is an important

part of the direct marketing approach. In order to support both the initial contact and the follow-up in direct marketing it is important that NASA develop the tools for use by their marketing personnel. These include presentation material of the type used in this study, as well as the various databases that can be used in the follow-up activity.

All of the above are elements of a marketing plan. In the absence of a marketing plan it is difficult to set goals or objectives for the marketing effort, to put in place the process to fulfill these goals or to even measure progress along the way. Based on the results of this study it may be concluded that the process of marketing to the biotechnology and pharmaceutical industries is a long-term effort, and that a carefully thought out plan for conveying information and following up with these industries is an important part of a future marketing effort. For this reason it is recommended that NASA consider the formulation of a long-term marketing plan for the biotechnology and pharmaceutical industries, and that consideration be given to direct marketing, along with other marketing tools, in the implementation of this plan.

APPENDIX A

LETTER TO CANDIDATE COMPANIES

ECON INCORPORATED

NINE HUNDRED STATE ROAD
PRINCETON, NEW JERSEY 08540
TELEPHONE 609 924-8778
TELEX 642-215

January 12, 1984

Dr. Zola Horovitz
E.R. Squibb
Box 4000
Princeton, NJ 08540

Dear Zola:

This letter will confirm our telephone conversation on January 11, 1984.

ECON, Inc., as a contractor to the National Aeronautics and Space Administration (NASA), is conducting a study of the potential use of the space environment by the U.S. pharmaceutical and biotechnology industries. A focus of the study is the access provided to the space environment by the NASA Space Shuttle. The principal objective of this study is to supply NASA with an independent assessment of the perceptions and needs of these industries concerning the potential use of the space environment for the processing of biological and pharmaceutical materials.

In order to perform this study, we plan to meet with a selected group of companies that may have an interest in the long term in the use of the space environment. We believe that E.R. Squibb may be such a company, and we solicit your cooperation and participation. The meeting will provide for an exchange of information. We will describe our understanding of the background and experience gained by NASA in their experimental work with the separation of biological materials in the space environment, the capabilities and facilities that can be made available by NASA to support this type of research and development as well as the range of working relationships that are possible with NASA. Through further discussion with you, we would then hope to gain additional insight into your attitudes, expectations and perceptions concerning the possible use of the space environment to support your research and development needs. These insights will be particularly useful to us in developing recommendations for actions that might be taken by NASA to make the use of the space environment more attractive to your industry.

It is our plan to hold individual meetings with the companies that participate in this study during February 1984. The meeting will be held at your facility, or at any location that is convenient to you. The duration of the meeting will be about two hours. After we complete our assessment of the results of the meetings, we may find it helpful to have a follow-up telephone conversation. Needless to say, we are not seeking proprietary information, and will treat any information that you would prefer to remain confidential (including the name of the company and respondent) as such in our final report to NASA.

Your participation in this study has two advantages. First, you will have an opportunity to get an overview of the prior work supported by NASA, and the capabilities of NASA facilities to support research and development in the separation of biological materials in the space environment. Second, you have an opportunity to provide an important input to the development of our recommendations to NASA concerning actions that they might take to make the space environment more accessible and productive to your industry. Upon final approval by NASA for distribution, we will provide you with a complimentary copy of the final report on the study.

I will call you in the next few days to answer any questions that you may have and to firm up the arrangements for a meeting in early February.

Best Regards,

B.P. Miller
President

BPM/md

APPENDIX B

BROCHURE USED IN MEETINGS WITH BIOTECHNOLOGY AND PHARMACEUTICAL COMPANIES

THE POTENTIAL USE OF THE SPACE ENVIRONMENT FOR THE PROCESSING OF BIOLOGICAL MATERIALS

A BACKGROUND BRIEFING FOR INDUSTRY

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THE INFORMATION CONTAINED IN THIS BRIEFING HAS BEEN PREPARED BY ECON, INC. UNDER CONTRACT NASW-3339 WITH THE NATIONAL AERONAUTICS AND SPACE ADMINISTRATION (NASA). THIS INFORMATION HAS BEEN OBTAINED FROM A LARGE NUMBER OF SOURCES. THE ASSEMBLY AND INTERPRETATION OF THE INFORMATION PRESENTED IN THIS DOCUMENT IS SOLELY AND EXCLUSIVELY THE RESPONSIBILITY OF ECON, INC. THIS DOCUMENT IS NOT MEANT TO SUPERSEDE OFFICIAL NASA PUBLICATIONS, AND HAS NOT BEEN ENDORSED OR OTHERWISE APPROVED BY NASA.

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CONTENTS

1. INTRODUCTION

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BACKGROUND

WITH THE SUCCESSFUL COMPLETION OF ITS NINTH FLIGHT LATE IN 1983, THE NASA SPACE SHUTTLE HAS DEMONSTRATED THE RELIABILITY AND REPRODUCIBILITY OF PERFORMANCE OF AN OPERATIONAL SYSTEM. THE SHUTTLE WILL MOVE FURTHER IN THE DIRECTION OF FULL OPERATIONAL CAPABILITY WITH TEN FLIGHTS PLANNED IN 1984 AND 12 IN 1985. BY THE END OF 1985 ALL FOUR SHUTTLE ORBITERS WILL BE IN FULL USE. THE CAPABILITY OF THE SHUTTLE TO REVISIT AN ORBITING SPACECRAFT FOR RETRIEVAL AND REPAIR WILL BE DEMONSTRATED IN 1984 AND AGAIN IN 1985. THUS, BY THE END OF 1985 NASA WILL HAVE SHOWN AN OPERATIONAL CAPABILITY TO REVISIT, RETRIEVE OR TEND AN ALREADY ORBITING SPACECRAFT.

THE FIRST EXPERIMENT INVOLVING THE PROCESSING OF BIOLOGICAL MATERIALS IN SPACE TOOK PLACE IN THE APOLLO 14 MISSION IN 1971. SUBSEQUENT EXPERIMENTS WERE FLOWN IN 1972, 1973 and 1975. EXPERIMENTS IN THE ELECTROPHORETIC SEPARATION OF BIOLOGICAL MATERIALS WERE RESUMED IN SHUTTLE MISSIONS IN 1982 AND 1983, AND ARE PLANNED TO CONTINUE IN 1984.

WHILE THE SHUTTLE HAS DEMONSTRATED ITS CAPABILITY TO SUPPORT MATERIALS PROCESSING EXPERIMENTS, AND THE PREVIOUS EXPERIMENTS ARE INDICATIVE OF A LONG-TERM INTEREST IN EXPLORING THE ADVANTAGES OF THE SPACE ENVIRONMENT, THE QUESTION OF THE LIKELY EXTENT OF USE OF THE SPACE ENVIRONMENT BY THE BIOLOGICAL AND PHARMACEUTICAL INDUSTRIES REMAINS UNANSWERED.

BACKGROUND

- SHUTTLE HAS DEMONSTRATED AN OPERATIONAL CAPABILITY
- SHUTTLE TENDED SPACECRAFT CAN BE A REALITY IN THIS DECADE
- BIOLOGICAL AND PHARMACEUTICAL MATERIALS PROCESSING EXPERIMENTS IN EARLIER PROGRAMS AND MISSIONS
- PHARMACEUTICAL INDUSTRY CONDUCTS AN AGGRESSIVE NEW PRODUCT RESEARCH AND DEVELOPMENT PROGRAM

IS THERE A MARKET FOR THE USE OF SPACE IN THE NEXT DECADE BY THE U.S. PHARMACEUTICAL INDUSTRY?

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OBJECTIVES OF THIS STUDY

IN THE PAST TWO DECADES SEVERAL CIVILIAN COMMERCIAL USES OF THE SPACE ENVIRONMENT HAVE BEEN EXPLORED AND HAVE DEVELOPED, IN BOTH THE PUBLIC AND PRIVATE SECTORS, AS OPERATIONAL SYSTEMS OR SUCCESSFUL COMMERCIAL VENTURES. THESE INCLUDE THE USE OF SPACE SYSTEMS FOR COMMUNICATION, NAVIGATION AND THE OBSERVATION OF THE EARTH AND ITS WEATHER. THESE APPLICATIONS HAVE ACHIEVED A SUFFICIENT DEGREE OF MATURITY SO THAT THE MARKET FOR TRANSPORTATION TO DELIVER SATELLITES TO ORBIT TO PERFORM THESE SERVICES IS RELATIVELY WELL UNDERSTOOD. THE USE OF THE SPACE ENVIRONMENT FOR THE PROCESSING OF BIOLOGICAL MATERIALS WAS SUGGESTED IN THE 1960s AND THE FIRST EXPERIMENT INVOLVING THE SEPARATION OF BIOLOGICAL MATERIALS IN THE SPACE ENVIRONMENT WAS CONDUCTED IN 19[illegible]. SINCE THAT TIME THERE HAVE BEEN SEVERAL EXPERIMENTS CONDUCTED BY NASA, AND RECENTLY BY MCDONNELL-DOUGLAS AND JOHNSON AND JOHNSON IN THE SPACE SHUTTLE. HOWEVER, THE USE OF THE SPACE ENVIRONMENT FOR THE PROCESSING OF BIOLOGICAL AND PHARMACEUTICAL MATERIALS HAS NOT MATURED AS RAPIDLY AS THE PREVIOUSLY MENTIONED APPLICATIONS. AS A RESULT, THERE IS A GREAT DEAL OF UNCERTAINTY CONCERNING THE POTENTIAL REQUIREMENTS OF THE BIOLOGICAL AND PHARMACEUTICAL INDUSTRIES. THE OBJECTIVES OF THIS STUDY ARE TO PROVIDE NASA WITH AN INDEPENDENT ASSESSMENT OF THE POTENTIAL NEEDS OF THESE INDUSTRIES FOR THE USE OF THE SPACE ENVIRONMENT, AND TO HELP NASA FORMULATE POLICIES THAT MIGHT MAKE THE USE OF THE SPACE ENVIRONMENT MORE ATTRACTIVE TO THE BIOLOGICAL AND PHARMACEUTICAL INDUSTRIES.

OBJECTIVES OF THIS STUDY

- ASSESS THE NEEDS AND PERCEPTIONS OF THE BIOTECHNOLOGY AND PHARMACEUTICAL INDUSTRIES RELATIVE TO THE POTENTIAL USE OF THE SPACE ENVIRONMENT AND THE SPACE SHUTTLE
- IDENTIFY ACTIONS THAT MIGHT BE TAKEN BY NASA TO MAKE THE USE OF THE SPACE ENVIRONMENT MORE ATTRACTIVE

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2. REVIEW OF FLIGHT EXPERIME[illegible]

A BASIS FOR INTEREST IN THE SPACE ENVIRONMENT

ELECTROKINETIC SEPARATION TECHNIQUES SUCH AS ELECTROPHORESIS, ISOELECTRIC FOCUSING, AND ISOTACHOPHORESIS ARE RESTRICTED IN THE LEVEL OF RESOLUTION THAT CAN BE ATTAINED AND/OR THE QUANTITY OF MATERIALS THAT CAN BE SEPARATED ON EARTH BECAUSE OF THE GRAVITY RELATED PHENOMENA OF SEDIMENTATION AND THERMAL CONVECTION. PROCESSING IN A LOW GRAVITY ENVIRONMENT ELIMINATES THESE GRAVITATIONALLY INDUCED EFFECTS AND MAY ALLOW FOR GREATER RESOLUTION AND YIELD OF PROCESSED MATERIALS. SEVERAL SEPARATION PROCESSES HAVE BEEN IDENTIFIED AS GOOD CANDIDATES FOR SPACE EXPERIMENTATION AND ARE DESCRIBED BELOW.

ELECTROPHORESIS IS THE TRANSPORT OF ELECTRICALLY CHARGED PARTICLES UNDER THE INFLUENCE OF A DIRECT CURRENT ELECTRICAL FIELD. THE PARTICLES WILL MIGRATE AT DIFFERENT RATES DEPENDING ON THEIR SURFACE CHARGE TOWARDS AN ELECTRODE WITH AN OPPOSITE CHARGE. MOST BIOLOGICAL MATERIALS WHEN DISSOLVED OR SUSPENDED IN AN AQUEOUS SOLUTION ACQUIRE A CHARACTERISTIC ELECTRICAL CHARGE DUE TO THE IONIZATION OF THEIR FUNCTIONAL GROUPS, ION ADSORPTION OR OTHER PHENOMENA AND THEIR MIGRATION VELOCITY PER UNIT ELECTRIC FIELD (ELECTROPHORETIC MOBILITY) IS FIXED IN A GIVEN BUFFER. ELECTROPHORETIC MOBILITY IS A COMPLEX FUNCTION OF THE PARTICLE'S ELECTRIC CHARGE, MOLECULAR SIZE, SHAPE, HYDRATION AND THE CHARACTERISTICS OF THE SOLVENT.

ELECTROPHORESIS IS SUBJECT TO SIGNIFICANT PROBLEMS, MANY CAUSED BY GRAVITY. LARGE BIOLOGICAL PARTICLES OF HIGH DENSITY SETTLE TO THE BOTTOM OF ELECTROPHORESIS BEDS AND CANNOT BE EFFECTIVELY SEPARATED. CONCENTRATIONS OF THE MATERIAL BEING SEPARATED MUST BE LIMITED BECAUSE HIGH CONCENTRATIONS WILL ADD TO THE DENSITY OF SUPPORTING ELECTROLYTE AND THIS DENSITY DIFFERENCE CAN RESULT IN GRAVITY DRIVEN CONVECTION. THUS THE THROUGHPUT MUST BE LIMITED. ANOTHER COMPLICATION IS THAT THE ELECTRIC FIELD CAUSES HEATING WITHIN THE MEDIUM WHICH CAN CAUSE THERMAL CONVECTION IN GROUND BASED PROCESSING PRODUCING FLOWS THAT DISRUPT THE MOVEMENT OF THE PARTICLES AND IMPAIR THE QUALITY OF THE SEPARATIONS. METHODS TO LIMIT THESE EFFECTS ON EARTH INCLUDE APPLYING LOW ELECTRIC FIELDS, (WHICH RESTRICTS THE DEGREE OF SEPARATION) AND USING THIN FLOW CHAMBERS SO THE HEAT CAN DISSIPATE THROUGH THE WALLS (WHICH LIMITS THROUGHPUT AND CAN CAUSE DISTORTIONS FROM WALL EFFECTS). SPACE PROCESSING MAY ELIMINATE THE NEED FOR THESE RESTRICTIVE METHODS.

ISOELECTRIC FOCUSING UTILIZES A VOLTAGE GRADIENT TO SET UP A pH GRADIENT IN THE BUFFER SOLUTION. MOBILITY OF THE PARTICLE VARIES AS A FUNCTION OF THE pH OF THE BUFFER. THE ISOELECTRIC POINT IS THE VALUE OF pH AT WHICH THE PARTICLE'S MOBILITY IS ZERO. PARTICLES MIGRATE TO THEIR ISOELECTRIC POINTS AND REMAIN THERE IMMOBILIZED. ISOELECTRIC FOCUSING IS AFFECTED BY SEDIMENTATION PROBLEMS AND GRAVITY-INDUCED CONVECTION. EVEN SLIGHT ELECTRO-OSMOSIS CAN SEVERELY EFFECT THE ISOELECTRIC FOCUSING PROCESS.

ISOTACHOPHORESIS DIFFERS FROM ORDINARY ELECTROPHORESIS IN THAT THE SAMPLE IS INSERTED BETWEEN TWO BUFFERS. THE LEADING BUFFERS' ANIONS HAVE GREATER ELECTROPHORETIC MOBILITY THAN THE SAMPLE AND THE TRAILING BUFFERS' ANIONS HAVE LESS MOBILITY. WHEN VOLTAGE IS APPLIED THE DIFFERENT COMPOUNDS TEND TO FORM SHARP DISTINCT BANDS ACCORDING TO THE MOBILITY OF THE ANIONS. BANDS PROGRESS AT EQUAL VELOCITY THROUGH THE COLUMN AND OVER THE COURSE OF MIGRATION, SAMPLE IONS ARE ARRANGED IN ORDER OF DECREASING MOBILITY. ANY MOLECULE THAT DIFFUSES ACROSS THE INTERFACE IS AUTOMATICALLY RETURNED TO THE REGION CORRESPONDING TO ITS MOBILITY. IF CONVECTIVE MIXING COULD BE ALLEVIATED, THIS METHOD COULD PROVIDE EXTREMELY HIGH RESOLUTION.

IN PHASE SEPARATION (COUNTER CURRENT DISTRIBUTION) CELLS TO BE SEPARATED ARE MIXED WITH TWO IMMISCIBLE LIQUIDS. DEPENDING ON ITS SURFACE PROPERTIES, THE CELL USUALLY SHOWS A PREFERENCE FOR ONE PHASE OVER THE OTHER. ON EARTH, SEDIMENTATION INTERFERES WITH SEPARATION BECAUSE THE DROPLETS SEDIMENT BEFORE PARTITIONING REACHES EQUILIBRIUM. BECAUSE SEDIMENTATION IS REDUCED IN SPACE A STABLE LIQUID SUSPENSION MAY BE MAINTAINED LONG ENOUGH TO ACHIEVE FULL PARTITIONING. AN ELECTRIC FIELD MUST BE APPLIED ACROSS THE FLUID TO INDUCE SEPARATION SINCE THE PHASES DON'T READILY SEPARATE.

A BASIS FOR INTEREST IN THE SPACE ENVIRONMENT

- SEPARATION TECHNIQUES ARE OFTEN USED IN RESEARCH AND/OR PRODUCTION PROCESSING OF BIOLOGICAL MATERIALS

  ELECTROPHORESIS

  ISOELECTRIC FOCUSING

  ISOTACHOPHORESIS

  LIQUID PHASE PARTITIONING

- ON EARTH, GRAVITY EFFECTS LIMIT THE CONCENTRATION AND PURITY OF BIOLOGICAL SAMPLES THAT CAN BE SEPARATED

  + SEDIMENTATION
  + CONVECTION

ANALYSIS AND MORE THAN TEN YEARS OF EXPERIMENTATION HAS SHOWN THAT CONCENTRATION AND PURITY CAN BE INCREASED IN THE SPACE MICROGRAVITY ENVIRONMENT

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WHAT DOES THE SPACE ENVIRONMENT OFFER TO THE BIOLOGICAL/PHARMACEUTICAL COMPANIES

SEDIMENTATION AND CONVECTION SEVERELY LIMIT THE CONCENTRATIONS AND PURITY OF THE BIOLOGICAL SAMPLES THAT CAN BE SEPARATED ON EARTH. IN A MICROGRAVITY ENVIRONMENT WHERE SEDIMENTATION AND CONVECTION ARE REDUCED OR ELIMINATED, IT MAY BE POSSIBLE TO ACHIEVE IMPROVED THROUGHPUT AND PURITY. WITHOUT SEDIMENTATION EFFECTS, THE SOLUTE BEING SEPARATED CAN BE PRESENT IN HIGH CONCENTRATIONS, WHICH WOULD ALLOW FOR INCREASED THROUGHPUT. WITHOUT THERMAL CONVECTION, THE CHAMBER WALLS CAN BE FURTHER APART PERMITTING A GREATER THROUGHPUT AND REDUCING DISTORTIONS FROM WALL EFFECTS, THEREBY INCREASING RESOLUTION. ALSO, BECAUSE THE APPLIED FIELD DOES NOT HAVE TO BE LIMITED, BETTER SEPARATIONS MAY BE ATTAINED.

WHAT DOES THE SPACE ENVIRONMENT OFFER TO THE BIOLOGICAL/PHARMACEUTICAL INDUSTRIES?

ENVIRONMENTAL ATTRIBUTE	EFFECT OF INTEREST	SEPARATION PROCESS SPECIFIC EFFECTS	END EFFECT	COMMENTS
MICROGRAVITY	ABSENCE OF GRAVITY-INDUCED EFFECTS	REDUCES OR ELIMINATES SEDIMENTATION AND CONVECTION EFFECTS	IMPROVED THROUGHPUT AND PURITY	CAN BE ACHIEVED ON OR NEAR EARTH FOR SECONDS TO MINUTES, IN ORBIT FOR DAYS TO MONTHS
HARD VACUUM	CLEAN ENVIRONMENT	REDUCES POSSIBILITIES OF CONTAMINATION	IMPROVED PURITY	CAN BE ACHIEVED ON EARTH-BASED FACILITIES, BUT CAN BE ACHIEVED IN CONJUNCTION WITH MICROGRAVITY ONLY IN SPACE
RADIATION	ELECTROMAGNETIC AND PARTICULATE RADIATION	—	—	NO USE FOR THIS ENVIRONMENTAL ATTRIBUTE HAS BEEN SUGGESTED IN CONNECTION WITH SEPARATIVE PROCESSES

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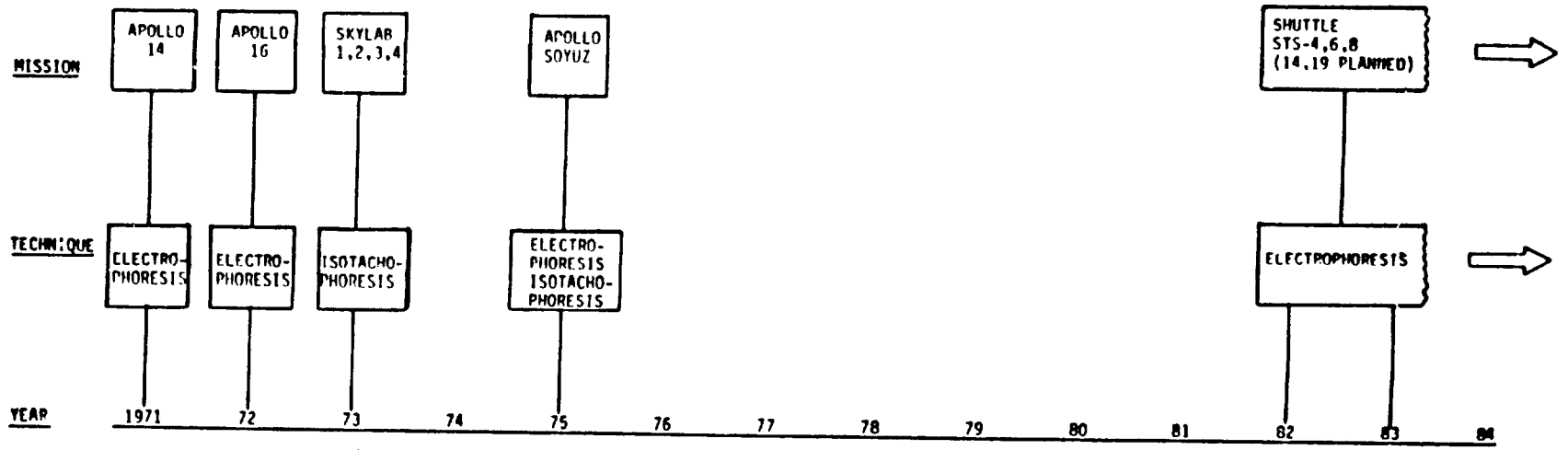
TIMELINE FOR SPACE BIOLOGICAL SEPARATION EXPERIMENTS

A NUMBER OF EXPERIMENTS HAVE BEEN CARRIED OUT IN SPACE, BEGINNING WITH AN ELECTROPHORESIS RUN ON APOLLO 14 IN 1971. THE EARLY EXPERIMENTS, ON APOLLOS 14 (1971) AND 16 (1972), SKYLAB (1973) AND APOLLO-SOYUZ (1975), DEMONSTRATED ENCOURAGING RESULTS IN SUPPORTING THE CONTENTION THAT SEPARATIONS PERFORMED IN SPACE MAY YIELD HIGHER RESOLUTIONS AND GREATER THROUGHPUT THAN CAN BE ATTAINED ON EARTH. HOWEVER, THESE EXPERIMENTS WERE LIMITED BY EQUIPMENT AND INSTRUMENTATION PROBLEMS. SUBSTANTIAL PROGRESS SEEMS TO HAVE BEEN MADE IN THE LONG GAP BETWEEN THE APOLLO-SOYUZ ELECTROPHORESIS EXPERIMENTS AND THE RECENT EXPERIMENTS RUN BY MCDONNELL-DOUGLAS IN THE SPACE SHUTTLE. IN THE INTERIM PERIOD PROGRESS HAS BEEN MADE IN UNDERSTANDING THE THEORY THROUGH MATHEMATICAL MODELING AND EXPERIMENTS CONDUCTED ON EARTH.

TIMELINE FOR SPACE BIOLOGICAL SEPARATION EXPERIMENTS



COMMENTS

ENCOURAGING RESULTS, BUT EXPERIMENTS LIMITED BY EQUIPMENT AND INSTRUMENTATION PROBLEMS

FIRST PRECOMMERCIAL EXPERIMENTS BY MDAC/J&J, AND EXPERIMENTS PERFORMED FOR NASA GOOD RESULTS REPORTED

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APOLLO 14

ACTUAL ON-ORBIT ELECTROPHORESIS EXPERIMENTATION BEGAN IN EARLY 1971 WITH AN ELECTROPHORESIS DEMONSTRATION ON APOLLO 14.

THE THREE MATERIALS SELECTED; RED AND BLUE DYE MIXTURE, HEMOGLOBIN AND SALMON SPERM DNA REPRESENTED A BROAD RANGE OF MOLECULAR WEIGHTS. THE OBJECTIVE WAS TO OBSERVE THE SHAPE AND DISTORTIONS OF THE SAMPLE BAND AS IT PROGRESSED UNDER THE INFLUENCE OF THE APPLIED FIELD. DATA WERE ACQUIRED BY PHOTOGRAPHY.

POOR LIGHTING AND CAMERA POSITIONING PROBLEMS IMPAIRED THE PHOTOGRAPHS, BUT THE SEPARATION OF THE RED AND BLUE DYES WAS DISCERNABLE IN THE PHOTOS. DENSITOMETER MEASUREMENTS MADE ON THE PHOTOS INDICATED THAT THE BOUNDARY BETWEEN THE DYES WAS SHARPER AND BETTER DEFINED THAN THAT OBTAINABLE IN A LIQUID COLUMN UNDER SIMILAR CONDITIONS ON EARTH. PHOTOGRAPHS TAKEN OF THE SPACE EXPERIMENT DID NOT SHOW LATERAL MOTION DUE TO THERMAL CONVECTION OR SEDIMENTATION AS WAS EVIDENT IN SIMILAR EXPERIMENTS PERFORMED ON EARTH.

ELECTROOSMOTIC FLOW ALONG THE COLUMN CAUSED SEVERE DISTORTION OF THE SAMPLE BAND. A SLIDE VALVE MALFUNCTION PUT THE DYE SAMPLE IN THE REGION OF MAXIMUM ELECTROOSMOTIC SHEAR RATHER THAN IN THE CENTER WHERE THE ELECTROOSMOTIC BAND BROADENING WOULD HAVE BEEN ONE-THIRD AS GREAT.

THE BIOLOGICAL SAMPLES WERE COMPLETELY DESTROYED BY BACTERIA, POSSIBLY DURING THE LONG STORAGE PERIOD BEFORE THE FLIGHT. THE UNIT WORKED AS DESIGNED AND WAS LATER REUSED.

APOLLO 16

A SECOND EXPERIMENT WAS CARRIED OUT IN 1972 ON APOLLO 16, USING AN APPARATUS SIMILAR TO THAT USED ON APOLLO 14. THE PHOTOGRAPHIC SETUP WAS ALTERED AND THE SAMPLE INJECTION SYSTEM REDESIGNED TO PROVIDE A SMOOTHER, MORE RELIABLE RELEASE OF SAMPLES. DATA COLLECTION WAS VIA PHOTOGRAPHS AND ASTRONAUTS COMMENTARY.

MONODISPERSE POLYSTYRENE LATEX PARTICLES WAS CHOSEN BECAUSE ITS ELECTROPHORETIC MOBILITY IS WELL KNOWN AND IT IS A GOOD MODEL FOR LIVE BIOLOGICAL MATERIALS.

ELECTROPHORESIS WAS ACHIEVED WITHOUT CONVECTION, BUT THERE WERE PROBLEMS WITH ELECTROOSMOTIC FLOW AND BUBBLES. THE CAUSE OF THE BUBBLES WAS ATTRIBUTED TO THE PERMEABILITY OF THE SILICON TUBING SUBJECTED TO THE RAPID EXTERNAL DEPRESSURIZATION OF AN APOLLO FLIGHT. FLUID DISTURBANCES ALSO DEVELOPED, CAUSING ONE OF THE MIGRATING ZONES TO TAKE ON A CORKSCREW APPEARANCE.

A SLIGHT SEPARATION OF THE LATEX MIXTURE WAS DISTINGUISHABLE USING SENSITIVE PHOTOGRAPHIC TECHNIQUES, DESPITE THE DISTORTION PRODUCED BY ELECTROOSMOSIS.

APOLLO FLIGHT EXPERIMENTS

APOLLO FLIGHT	14	16
TECHNIQUE	ELECTROPHORESIS	ELECTROPHORESIS
MATERIALS	• RED AND BLUE DYE • HEMOGLOBIN • SALMON SPERM DNA	MONODISPERSED POLYSTYRENE LATEX SPHERES
INSTRUMENTATION	• PHOTOGRAPHIC • NO SEPARATION COLLECTION	• PHOTOGRAPHIC • ASTRONAUT COMMENTARY
ACCOMPLISHMENTS	• BETTER SEPARATION THAN UNDER SIMILAR CONDITIONS ON GROUND	• ELECTROPHORESIS ACHIEVED WITHOUT CONVECTIVE EFFECTS
PROBLEMS	• LIGHTING AND CAMERA POSITION • VALVE MALFUNCTION • ELECTROOSMOSIS • BIOLOGICAL SAMPLES DESTROYED BY BACTERIA	• ELECTROOSMOSIS • BUBBLES IN FLOW FIELD ATTRIBUTED TO SILICON TUBING • FLUID DISTURBANCE OF UNKNOWN NATURE
PRINCIPAL INVESTIGATOR	E. C. MC KANNAN MARSHALL SPACE FLIGHT CENTER	

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SKYLAB EXPERIMENT TV117

AN ATTEMPT WAS MADE TO SEPARATE HUMAN RED BLOOD CELLS AND TWO PROTEINS, FERRATIN AND HEMOGLOBIN USING ISOTACHOPHORESIS ON SKYLAB. THE OBJECTIVE WAS TO DETERMINE WHETHER LOW GRAVITY COULD ALLEVIATE CONVECTIVE MIXING AND SEDIMENTATION PROBLEMS THAT ARE ASSOCIATED WITH SEPARATIONS IN ONE-GRAVITY AND ACHIEVE PROTEIN SEPARATIONS TO COMPARE WITH GEL TECHNIQUES, AND TO DETERMINE WHETHER LARGER PARTICLES SUCH AS CELLS COULD BE SEPARATED BY THIS PROCESS.

THE PROTEIN SEPARATION FAILED. A SMALL AMOUNT OF AIR HAD ENTERED THE SYSTEM THROUGH SLIGHT LEAKS THAT HAD DEVELOPED. A GAS BUBBLE FORMED, ISOLATING THE ELECTRODE AND PREVENTING THE CURRENT FROM FLOWING.

THE TUBE WITH RED BLOOD CELLS PRODUCED BETTER RESULTS, ALTHOUGH THE PROCESS WAS AFFECTED BY ELECTROOSMOSIS.

SKYLAB EXPERIMENT TV117

TECHNIQUE	ISOTACHOPHORESIS
MATERIALS	• HUMAN RED BLOOD CELLS • A MIXTURE CONTAINING TWO PROTEINS: FERRITIN AND HEMOGLOBIN
PROBLEMS	• PROTEIN SEPARATION FAILED BECAUSE A SMALL AMOUNT OF AIR HAD ENTERED THE SYSTEM THROUGH SLIGHT LEAKS THAT HAD DEVELOPED. A GAS BUBBLE FORMED AND ISOLATED THE ELECTRODE PREVENTING THE CURRENT FROM FLOWING. • THE RED BLOOD CELL SEPARATION WAS AFFECTED BY ELECTROOSMOSIS
PRINCIPAL INVESTIGATOR	DR. MILAN BIER UNIVERSITY OF ARIZONA

APOLLO-SOYUZ MA-011 (US)

EXPERIMENT MA-011 WAS A STATIC ELECTROPHORESIS SYSTEM DESIGNED FOR TESTING BOTH ELECTROPHORESIS AND ISOTACHOPHORESIS. THE EQUIPMENT DEVELOPED FOR THE APOLLO EXPERIMENTS WAS EXTENDED AND COMBINED WITH NEW SAMPLE HANDLING PROCEDURES TO WORK WITH BIOLOGICAL MATERIALS. THE EXPERIMENT USED EIGHT SAMPLE INSERTION SLIDES, TWO OF EACH OF THE FOLLOWING: A MIXTURE OF ALDEHYDE FIXED RED BLOOD CELLS FROM HUMAN, RABBIT AND HORSE, HUMAN PERIPHERAL BLOOD LYMPHOCYTES, HUMAN FETAL KIDNEY CELLS, RABBIT AND HUMAN RED BLOOD CELLS, (ONE COLUMN FIXED AND ONE FROZEN WHICH WERE USED FOR THE ISOTACHOPHORESIS EXPERIMENT.) THE SAMPLES WERE FROZEN IN LIQUID NITROGEN UP UNTIL BEING USED, AND AT THE END OF THE RUN THE COLUMNS WERE FROZEN IN-SITU AND RETURNED TO EARTH IN LIQUID NITROGEN.

THE EXPERIMENT SHOWED THAT SPACE ELECTROPHORESIS CAN PROVIDE CAPABILITIES NOT AVAILABLE ON EARTH. POSTFLIGHT ANALYSES OF A RED BLOOD CELL SEPARATION AND A SEPARATION OF CORTICAL KIDNEY CELLS SHOW THAT THE APPARATUS SUCCESSFULLY TRANSPORTED SAMPLES OVER DISTANCES OF ABOUT 10 CM WITHOUT SERIOUS DISTURBANCES FROM FLUID FLOW, A CAPABILITY, POSSESSED BY NO EARTH-BASED APPARATUS. THE RED BLOOD CELL SEPARATION ACHIEVED SHARP PARTICLE BAND BOUNDARIES, AND MIGRATION AGREED WITH THE PREDICTED MIGRATION IN GENERAL. THE SEPARATED KIDNEY CELLS WERE CULTURED UPON RETURN TO EARTH AND SOME OF THE KIDNEY CELL FRACTIONS SHOWED ENHANCED PRODUCTION OF PRODUCTS SUCH AS UROKINASE, HUMAN GRANULOCYTE STIMULATING HORMONE AND ERYTHROPOIETIN , INDICATING THAT SOME CELLS MAY BE PRODUCT SPECIFIC. ANOTHER ACHIEVEMENT WAS THE PREVENTION OF ELECTROOSMOSIS BY THE USE OF A LOW ZETA POTENTIAL COLUMN COATING. THE EQUIPMENT MET OBJECTIVES AND SATISFACTORY SAMPLE COLLECTION, RETURN AND PRESERVATION TECHNIQUES WERE DEMONSTRATED. CONTAMINATION WAS AVOIDED.

UNFORTUNATELY ENGINEERING AND OPERATIONAL PROBLEMS COMPROMISED SEVERAL OF THE RUNS ATTEMPTED. FLUID LINE BLOCKAGES CAUSED MALFUNCTIONS IN ONE OF THE FIXED RED BLOOD CELL COLUMNS, AND BOTH LYMPHOCYTE COLUMNS. ONE KIDNEY CELL COLUMN DEVELOPED A LEAK DURING PROCESSING. ONE FROZEN CYLINDER OF RED BLOOD CELLS FRACTURED AS IT WAS BEING SLICED ON EARTH AND ANALYSES INDICATE THE SAMPLE WAS MIXED OR CONTAMINATED.

THE ISOTACHOPHORESIS RUN DEMONSTRATED THE ADVANTAGE OF ISOTACHOPHORESIS IN THE SHARPNESS OF THE FRONTAL BOUNDARY AND CONCENTRATION OF THE MIGRATING ZONES. IN THE EXPERIMENT WITH THE FIXED RED CELLS, THE PHOTOGRAPHY WASN'T GOOD ENOUGH TO SHOW THE WHOLE COLUMN LENGTH. ONLY FOUR FRAMES WERE AVAILABLE FOR EVALUATION AND SHOW THAT OVERALL MIGRATION WAS SOMEWHAT LOWER THAN PREDICTED. IN THE COLUMN OF NATIVE UNFIXED RED CELLS THE OVERALL MIGRATION WAS 60 PERCENT OF THAT PREDICTED AND ONLY THE LAST FOUR PHOTOS SHOW ANY TRACE OF THE SAMPLE. SEPARATION COULD NOT BE CONCLUDED BECAUSE THE REAR BOUNDARIES WEREN'T SEEN BECAUSE OF INSUFFICIENT MIGRATION DISTANCE. THE INSUFFICIENT DURATION OF THE RUN (45 MINUTES) PREVENTED THE BANDS FROM COMING INTO FULL VIEW.

APOLLO SOYUZ MA-011 (US)

TECHNIQUE	ELECTROPHORESIS	ISOTACHOPHORESIS
MATERIALS	• RED BLOOD CELLS FROM HUMAN, RABBIT AND HORSE • HUMAN PERIPHERAL BLOOD LYMPHOCYTES • HUMAN FETAL KIDNEY CELLS	• FIXED RABBIT AND HUMAN RED BLOOD CELLS • FROZEN RED BLOOD CELLS
INSTRUMENTATION	• PHOTOGRAPHIC • SEPARATION COLLECTION	• PHOTOGRAPHIC
ACCOMPLISHMENTS	• A LOW ZETA POTENTIAL COLUMN COATING SUCCESSFULLY ELIMINATED ELECTROOSMOSIS • ELECTROPHORESIS OF ALDEHYDE FIXED RED BLOOD CELLS ACHIEVED SHARP PARTICLE BAND BOUNDARIES AND IN GENERAL OBSERVED MIGRATION AGREED WITH PREDICTED MIGRATION • KIDNEY CELL SEPARATIONS INDICATED THAT SEPARATED CELLS APPEARED TO BE PRODUCT SPECIFIC • SATISFACTORY SAMPLE COLLECTION, RETURN AND PRESERVATION TECHNIQUES • THE ELECTROPHORESIS UNIT ALLOWED FOR TWO DIFFERENT TYPES OF SEPARATIONS TO BE CONDUCTED AND ALLOWED FOR A MULTIPLE RUN CONDITION • THE ELECTROPHORESIS UNIT, CRYOGENIC FREEZER AND DATA COLLECTION ASSEMBLY MET OBJECTIVES WITH SATISFACTORY EXPERIMENTAL RESULTS • CONFIRMATION OF BIO COMPATIBILITY OF ALL APPROPRIATE HARDWARE COMPONENTS AND THE USE OF A STERILE OPERATING ENVIRONMENT • NO CONTAMINATION	• DEMONSTRATED SHARPNESS OF THE FRONTAL BOUNDARIES • THE ELECTROPHORESIS UNIT ALLOWED FOR TWO DIFFERENT TYPES OF SEPARATIONS TO BE CONDUCTED AND ALLOWED FOR A MULTIPLE RUN CONDITION • THE ELECTROPHORESIS UNIT, CRYOGENIC FREEZER AND DATA COLLECTION ASSEMBLY MET OBJECTIVES WITH SATISFACTORY EXPERIMENTAL RESULTS • CONFIRMATION OF BIO COMPATIBILITY OF ALL APPROPRIATE HARDWARE COMPONENTS AND THE USE OF A STERILE OPERATING ENVIRONMENT • NO CONTAMINATION
PROBLEMS	• CLOGGED FLUID CONNECT LINES IN ELECTRODE HOUSING CAUSED MALFUNCTIONS IN THREE OF THE RUNS • ONE COLUMN WALL FRACTURED DURING SLICING OPERATION • ONE KIDNEY CELL COLUMN DEVELOPED A LEAK THAT PRECLUDED ELECTROPHORESIS	• POOR PHOTOGRAPHIC RECORD • INSUFFICIENT DURATION OF THE RUN PREVENTED COLUMNS FROM COMING INTO FULL VIEW • NO EVIDENCE OF SEPARATION
PRINCIPAL INVESTIGATOR	DR. ROBERT SNYDER MARSHALL SPACE FLIGHT CENTER	

Econ

APOLLO-SOYUZ MA-014 (WEST GERMANY)

THIS EXPERIMENT SPONSORED BY THE GERMAN SPACE AGENCY WAS DESIGNED TO PERFORM CONTINUOUS FLOW ELECTROPHORESIS IN SPACE ON BIOLOGICAL CELL MATERIALS WITH REGARD FOR HIGH SAMPLE THROUGHPUTS AT HIGH RESOLUTION, AND TO CONTRIBUTE TO THE INVESTIGATION OF THERMAL AND CONVECTIVE PROPERTIES OF CHAMBERS WITH HIGH GAP WIDTH. THE MACHINE WAS DESIGNED TO WORK AUTOMATICALLY. RESULTS WERE EVALUATED BY SCANNING THE ADSORPTION PATTERN ACROSS THE SEPARATION GAP, DIGITIZING THE DATA AND STORING BOTH THE SCIENTIFIC AND HOUSEKEEPING DATA ON TAPE.

THE FOLLOWING SAMPLES WERE SEPARATED: RAT BONE-MARROW CELLS, RAT SPLEEN CELLS, MIXTURE OF RABBIT AND HUMAN ERYTHROCYTES, RAT LYMPH-NODE CELLS AND HUMAN ERYTHROCYTES. WHEN THE RECORDED DATA WAS EXAMINED IT WAS FOUND THAT THE LIGHT SOURCE (A HALOGEN LAMP) FOR THE ADSORPTION MEASURING OPTICS HAD BEEN EXCESSIVELY BRIGHT AND ADVERSELY AFFECTED THE MEASURING RANGE. THE REASON WAS THAT THE LAMP LACKED INTERNAL CONVECTION BECAUSE OF ZERO GRAVITY. AS A CONSEQUENCE IT WAS DIFFICULT TO INTERPRET THE RECORDED DATA.

HOWEVER, SOME CONCLUSIONS WERE POSSIBLE BECAUSE DURING THE STATIONARY PHASE IRREGULARLY OCCURRING PULSES WERE RECORDED WHOSE PATTERN REFLECTED THE EXPECTED COURSE OF THE SEPARATION CURVES. THE FOLLOWING CONCLUSIONS WERE DRAWN. THE BONE MARROW SAMPLE SHOWED AN EXCELLENT SEPARATION PATTERN THAT WAS SHARPER THAN THAT MEASURED BY COMPARABLE GROUND EQUIPMENT. THE BEST RESULTS WERE ACHIEVED WITH SPLEEN CELLS. THERE WAS SUFFICIENT DATA TO IDENTIFY THE DETAILS OF THE SEPARATION, AND THE PREDICTION OF HIGH SEPARATION QUALITY WITH HIGH-RATE SAMPLE PROCESSING WAS CONFIRMED. WELL FOUNDED RESULTS FROM THE ERYTHROCYTE SEPARATION WERE PRECLUDED BY LACK OF INFORMATION. LYMPH NODE CELLS SHOWED A SOMEWHAT POORER DISTRIBUTION DUE TO THE LACK OF INFORMATION STORED, BUT IN COMPARISON TO GROUND BASED WORK THE POSITIVE EFFECTS OF SPACE CONDITIONS WAS STRIKING. COMPARISON OF THE SEPARATION CURVES ACHIEVED IN SPACE WITH THOSE ACHIEVED IN GROUND TESTS INDICATED THE FAVORABLE EFFECT OF THE MICROGRAVITY ENVIRONMENT.

APOLLO-SOYUZ MA-014 (WEST GERMANY)

TECHNIQUE	CONTINUOUS FLOW ELECTROPHORESIS
MATERIALS	• RAT BONE MARROW CELLS • RAT SPLEEN CELLS • MIXTURE OF HUMAN AND RABBIT ERYTHROCYTES • RAT LYMPH-NODE CELLS AND HUMAN ERYTHROCYTES
INSTRUMENTATION	• SCANNING THE ABSORPTION PATTERN ACROSS THE SEPARATION GAP. DIGITIZING THE DATA AND STORING ON TAPE
ACCOMPLISHMENTS	• BONE MARROW SAMPLE SHOWED EXCELLENT SEPARATION PATTERN THAT WAS SHARPER THAN THAT MEASURED BY COMPARABLE GROUND EQUIPMENT • SPLEEN CELL SEPARATION OF HIGH QUALITY
PROBLEMS	• THE LIGHT SOURCE (A HALOGEN LAMP) FOR THE ABSORPTION MEASURING OPTICS WAS EXCESSIVELY BRIGHT AND ADVERSELY AFFECTED THE MEASURING RANGE. THIS CAUSED DIFFICULTIES INTERPRETING RECORDED DATA.
PRINCIPAL INVESTIGATOR	R. HANNIG MAX PLANCK INSTITUTE, MUNICH WEST GERMANY

A GENERAL OBSERVATION ON EARLY FLIGHT EXPERIMENTS

A NUMBER OF SEPARATION EXPERIMENTS HAVE BEEN DESIGNED FOR AND CARRIED OUT ON BOARD SPACE VEHICLES IN ORDER TO DETERMINE WHETHER SEPARATION PROCESSES CARRIED OUT IN A LOW GRAVITY ENVIRONMENT WOULD YIELD HIGHER LEVEL RESOLUTIONS AND GREATER QUANTITIES THAN WOULD PROCESSES SUBJECT TO THE GRAVITATIONALLY INDUCED EFFECTS OF SEDIMENTATION AND THERMAL CONVECTION. THESE EXPERIMENTS HAVE DEMONSTRATED THAT SEDIMENTATION AND THERMAL CONVECTION ARE DIMINISHED IN SPACE AS COMPARED WITH EARTH PROCESSING. YET, UNTIL THE SHUTTLE EXPERIMENTS ALMOST EVERY EXPERIMENT EXPERIENCED EQUIPMENT OR PROCEDURAL PROBLEMS. MECHANICAL DIFFICULTIES WERE EXPERIENCED SUCH AS CAMERA AND LIGHTING PROBLEMS ON APOLLO 14, FLUID BLOCKAGES IN SOME OF THE COLUMNS IN EXPERIMENT MA-011 ON APOLLO-SOYUZ, THE MALFUNCTIONING OF THE HALOGEN LAMP IN EXPERIMENT MA-014 ON APOLLO-SOYUZ, OR LEAKS THAT COMPROMISED THE SKYLAB ISOTACHOPHORESIS RUN.

IN GENERAL, EACH SUCCESSIVE EXPERIMENT APPEARS TO HAVE OVERCOME THE PROBLEMS OF THE PRECEDING ONES. ELECTROOSMOSIS DISTORTED SOME OF THE EARLIER EXPERIMENTS ON APOLLO 14 AND 16; IN LATER EXPERIMENTS ELECTROOSMOSIS WAS AVOIDED BY THE USE OF A SUITABLE ZERO-SURFACE-POTENTIAL MATERIAL. BACTERIA DESTROYED BIOLOGICAL SAMPLES ON APOLLO 14, BUT THIS WAS AVOIDED WITH LATER EXPERIMENTS.

EARLY EXPERIMENT RESULTS WERE ENCOURAGING AND SUPPORTED THE NOTION THAT LOW GRAVITY PROCESSING COULD YIELD HIGHER QUALITY AND GREATER QUANTITY SEPARATIONS. HOWEVER, THEY WERE ADVERSELY AFFECTED BY EQUIPMENT PROBLEMS. THE NEXT GENERATION OF EXPERIMENTS, THE SHUTTLE EXPERIMENTS, HAVE A BETTER EMPIRICAL AND THEORETICAL BASIS AND APPEAR TO BE CONSIDERABLY MORE SUCCESSFUL.

A GENERAL OBSERVATION ON EARLY FLIGHT EXPERIMENTS

- RESULTS WERE ENCOURAGING BUT NOT CONCLUSIVE IN TERMS OF IMPROVED PERFORMANCE OF SEPARATION TECHNIQUES IN THE SPACE ENVIRONMENT
- EXPERIMENTS WERE HAMPERED BY TEST EQUIPMENT AND INSTRUMENTATION PROBLEMS
- PROBLEMS SEEM TO BE SIMILAR TO THOSE ENCOUNTERED AND OVERCOME IN SATELLITE DESIGN IN THE EARLY DAYS OF THE SPACE PROGRAM (1957-65); I.E., DEVELOPMENT OF EQUIPMENT AND PROCEDURES THAT WORK RELIABLY IN THE SPACE ENVIRONMENT

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Econ

3. NASA CAPABILITIES TO SUPPORT SEPARATION RESEARCH IN A MICROGRAVITY ENVIRONMENT

NASA CAPABILITIES FOR MICROGRAVITY RESEARCH

A NUMBER OF NASA FACILITIES ARE AVAILABLE FOR INVESTIGATING THE EFFECTS OF NEAR-ZERO GRAVITY ON MATERIALS PROPERTIES AND PROCESSES. THESE FACILITIES CAN BE BROADLY CATEGORIZED INTO GROUND-BASED AND SPACE-BASED FACILITIES.

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NASA CAPABILITIES FOR MICROGRAVITY RESEARCH

CAPABILITIES INCLUDE:

- GROUND-BASED FACILITIES
- SPACE-BASED FACILITIES

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NASA GROUND BASED FACILITIES

NASA GROUND-BASED FACILITIES CONSIST OF A DROP TOWER, DROP TUBES, AIRCRAFT AND SOUNDING ROCKETS. THE DROP TOWER AND DROP TUBES CAN ATTAIN LOW GRAVITY FOR TWO TO FIVE SECONDS. THE DROP TOWER AND DROP TUBES ARE LOCATED IN MARSHALL SPACE FLIGHT CENTER, HUNTSVILLE, ALABAMA AND ARE OPERATIONAL. NASA ALSO HAS TWO AIRCRAFT - A KC-135 AT JOHNSON SPACE CENTER, AND A F-104 AT DRYDEN RESEARCH CENTER - THAT ARE USED TO SIMULATE NEAR-ZERO GRAVITY THROUGH PARABOLIC FLIGHT MANEUVERS.

THERE IS NOT YET ANY SET PROTOCOL FOR THE USE OF THESE FACILITIES. ALL REQUESTS FOR THEIR USE ARE HANDLED BY NASA ON A CASE-BY-CASE BASIS. THE COSTS OF USING THESE FACILITIES ARE DEPENDENT UPON THE AGREEMENT MADE WITH NASA.

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NASA GROUND-BASED FACILITIES
(NONORBITAL)

FACILITY	LOCATION	DURATION OF EXPOSURE TO REAL ZERO-G
DROP TOWER	MARSHALL SPACE FLIGHT CENTER, AL	5 SEC.
DROP TUBE	MARSHALL SPACE FLIGHT CENTER, AL	2 - 5 SEC.
AIRCRAFT • KC-135 • F-104	JOHNSON SPACE CENTER, TX. DRYDEN RESEARCH CENTER, CA	20 - 25 SEC. 60 SEC. (REPEATED SEVERAL TIMES PER FLIGHT)
SOUNDING ROCKETS	WHITE SANDS, NM	5 MIN

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- COST FOR USE OF FACILITY MAY RANGE FROM NO COST UNDER JOINT ENDEAVOR AGREEMENT TO REIMBURSEMENT FOR SHARE OF COST. EXPERIMENT PACKAGE SUPPLIED BY EXPERIMENTER.
- SHORT LEAD TIME CAN BE ARRANGED FOR USE OF FACILITIES.

DROP TUBES & DROP TOWER

ONE OF THE DROP TUBES AT MARSHALL IS A 30 M TUBE TOPPED BY A MELTING APPARATUS CONTAINED IN A BELL JAR. THE BELL JAR AND TUBE ASSEMBLY CAN EITHER BE EVACUATED TO LOW PRESSURES OR CAN BE BACK-FILLED WITH HELIUM. FREE FALL TIME IN THE 30 M TUBE IS 2.6 SECONDS. THERE ARE THREE MELTING APPARATUS AVAILABLE THAT CAN BE USED TO OBTAIN MELTING POINTS IN THE RANGE OF 600 C TO 3500 C. SAMPLE SIZES CAN VARY FROM 1 MM to 5 MM. A NEW 100 M DROP TUBE IS NOW ON-LINE AT MARSHALL.

THE DROP TOWER AT MARSHALL IS 100 M HIGH AND CAN ATTAIN A FREE FALL DURATION OF ABOUT 5 SECONDS. THE DIMENSION OF EXPERIMENTS THAT CAN BE DROPPED FROM THE DROP TOWER IS TYPICALLY 2' X 2 1/2' X 4'. THE EXPERIMENT PACKAGE ALLOWS FOR SOME PERIPHERIAL EQUIPMENT IN THE CORNERS.

DROP TUBES & DROP TOWER

- 30 METER LONG TUBE TOPPED BY A MELTING APPARATUS CONTAINED IN A BELL JAR
- BELL JAR AND TUBE ASSEMBLY CAN EITHER BE EVACUATED TO CREATE VACUUM OR CAN BE FILLED WITH HELIUM
- SAMPLE MELTING TEMPERATURE OF 600^{o}C TO 3500^{o}C
- SAMPLE SIZE OF 1 MM TO 5 MM
- ACCELERATION OF SAMPLE IN TUBE
  - $10^{-6}g$ IN VACUUM
  - $10^{-3}g$ IN HELIUM FILLED TUBE
- FREE FALL TIME OF 2.6 SECONDS
- NEW 100 M DROP TOWER ON-LINE AT MSFC
  - ACCOMMODATES TEST UNIT OF ABOUT 2' X 2 1/2' X 4'

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SOUNDING ROCKETS

SOUNDING ROCKETS ARE LAUNCHED FROM WHITE SANDS MISSILE RANGE IN NEW MEXICO. THE FLIGHT OF THE ROCKET CREATES A NEAR-ZERO GRAVITY CONDITION FOR THE PAYLOAD AT THE APOGEE OF THE TRAJECTORY FOR ABOUT FIVE MINUTES. THE DIMENSION OF THE PAYLOAD AREA IS APPROXIMATELY 17 INCHES IN OUTSIDE DIAMETER BY 4 FEET IN HEIGHT. THE EXPERIMENT PACKAGES THEMSELVES ARE LIMITED TO A DIAMETER OF 16 INCHES AND THE SHORTEST LENGTH POSSIBLE. THE MAXIMUM WEIGHT CARRIED PER FLIGHT IS 1000 LBS. THE INDIVIDUAL EXPERIMENTS ARE DUE AT MARSHALL FOUR MONTHS BEFORE FLIGHT TIME.

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SOUNDING ROCKETS

- PLANNED LAUNCHES TWICE A YEAR FROM WHITE SANDS MISSILE RANGE IN NEW MEXICO
  - + SPAR 9 - 1982
  - + SPAR 10 - 1983
- ATTAINS NEAR ZERO G FOR ABOUT FIVE MINUTES
- MAXIMUM TOTAL PAYLOAD WEIGHT ~ 1000 LBS.
- INDIVIDUAL EXPERIMENT LIMITATIONS ARE
  - + 16" DIAMETER x 4' HIGH
  - + AS SHORT AS POSSIBLE
  - + MAXIMUM PACKAGING DENSITY OF 60 LB./FT.^{3}

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AIRCRAFT

THERE ARE TWO AIRCRAFT AVAILABLE IN THE NASA SYSTEM THAT ARE USED TO CREATE NEAR-ZERO GRAVITY. THE FIRST IS A MILITARY VERSION OF THE BOEING 707 (KC-135) AND IS LOCATED AT JOHNSON SPACE CENTER IN HOUSTON, TEXAS. THE KC-135 ATTAINS NEAR-ZERO GRAVITY BY FLYING A PARABOLIC FLIGHT TRAJECTORY. NEAR-ZERO GRAVITY IS ATTAINED FOR ABOUT 25 SECONDS AND CAN BE REPEATED UP TO 50 TIMES PER FLIGHT. THE LARGE EQUIPMENT SPACE AVAILABLE IN THE KC-135, 60' X 10' X 7', ALLOWS FOR LARGE EXPERIMENTS AND HANDS-ON PERSONNEL. THE LEAD TIME FOR SCHEDULING EXPERIMENTS ON THE KC-135 VARIES FROM ONE TO SIX MONTHS.

THE SECOND IS AN F-104 AIRCRAFT, BASED AT DRYDEN RESEARCH CENTER, CALIFORNIA. THE F-104 ATTAINS NEAR-ZERO GRAVITY BY PERFORMING PARABOLIC FLIGHT TRAJECTORIES JUST AS THE KC-135 DOES. THE NEAR-ZERO GRAVITY PERIOD IS ABOUT 60 SECONDS IN DURATION AND CAN BE REPEATED A NUMBER OF TIMES. THE EXPERIMENT SIZE IS LIMITED TO AN AREA OF 23" HIGH X 14" WIDE X 11" DEEP. PART OF THIS SPACE IS TAKEN UP BY A POWER REGULATOR WHOSE DIMENSIONS ARE 12" X 3" X 6.5". THE MAXIMUM WEIGHT OF THE EXPERIMENTS THAT CAN BE CARRIED IS 70 LBS. EXPERIMENTS SHOULD BE AT MARSHALL TWO WEEKS BEFORE THE F-104 FLIGHT DATE.

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AIRCRAFT

AIRCRAFT TYPE / CHARACTERISTICS	KC-135	F-104
METHOD OF OBTAINING MICROGRAVITY	FLY PARABOLIC TRAJECTORY FROM 24,000 FEET TO 33,000 FEET AND BACK	FLY PARABOLIC TRAJECTORY FROM 25,000 FEET TO 65,000 FEET AND BACK
DURATION	20-25 SEC, REPEATED UP TO 50 TIMES PER FLIGHT	60 SEC, REPEATED SEVERAL TIMES PER FLIGHT
TEST EQUIPMENT SPACE	60' X 10' X 7'	23" X 14" X 11", INCLUDING 12" X 3" X 6.5" FOR POWER REGULATOR
TEST EQUIPMENT WEIGHT	LIMITED BY FLOOR LOADING OF 200#/ft^2	UP TO 70#

Econ

SPACE-BASED FACILITIES
(ORBITAL)

THE NASA SPACE SHUTTLE PROVIDES A WIDE RANGE OF ACCOMMODATIONS TO SUPPORT MATERIALS PROCESSING EXPERIMENTS IN THE SPACE ENVIRONMENT. THESE RANGE FROM SMALL SELF CONTAINED EXPERIMENTS THAT OPERATE IN AN AUTOMATED MANNER AND INTERFACE WITH THE SHUTTLE ONLY FOR POWER AND OPERATING MODE COMMANDS, TO LARGE COMPLEX EXPERIMENTS INSTALLED IN THE SHUTTLE PAYLOAD BAY AND OPERATED BY A MEMBER OF THE SHUTTLE FLIGHT CREW WORKING FOR THE ORGANIZATION THAT IS CONDUCTING THE EXPERIMENT. WITH ITS PRESENT OPERATING CAPABILITY THE SPACE SHUTTLE CAN PROVIDE UP TO TEN DAYS OF EXPOSURE TO THE NEAR-ZERO-g ENVIRONMENT. IN ADDITION, THE SHUTTLE IS CAPABLE OF DELIVERING AND REVISITING LARGE AUTOMATED SPACECRAFT IN NEAR-EARTH ORBIT. THESE LARGE ORBITING SPACECRAFT CAN PROVIDE EXPOSURE TO THE NEAR-ZERO-g ENVIRONMENT FOR LONGER PERIODS OF TIME.

SPACE-BASED FACILITIES
(ORBITAL)

PROGRAM	STATUS	CONTACT	COMMENTS	DURATION OF EXPOSURE TO NEAR ZERO-G
SMALL SELF-CONTAINED EXPERIMENTS	ACTIVE	DONNA MILLER NASA HEADQUARTERS WASHINGTON, DC	SEVERAL EXPERIMENTS HAVE FLOWN. POLICY IN PLACE.	10 DAYS
CAPACITY FOR OPPORTUNITY PAYLOAD EXPERIMENTS • MULTI-POSITIONARY EXPERIMENT SUPPORT STRUCTURE (MPESS) • COMMERCIAL SYSTEMS	PLANNING	JOHN MOYE ROBERT LOHMAN NASA HEADQUARTERS WASHINGTON, DC	CONCEPT IS IN DISCUSSION. POLICY FOR ACCESSING DOES NOT EXIST.	10 DAYS
SPACELAB • PALLETS • HABITABLE MODULES	ACTIVE	MICHAEL SANDER NASA HEADQUARTERS WASHINGTON, DC	FIRST FLIGHT STS-9. POLICY FOR COMMERCIAL USE NOT YET APPROVED.	10 DAYS
CREW COMPARTMENT AREAS (SHUTTLE)	ACTIVE	RONALD PHILIPS NASA HEADQUARTERS WASHINGTON, DC	MID-DECK USED BY MDAC/J&J. POLICY FOR COMMERCIAL USE NOT ESTABLISHED.	10 DAYS
PAYLOAD BAY (15 FT. DIA. X 60 FT. LONG) (SHUTTLE)	ACTIVE	CHESTER LEE CUSTOMER SERVICES NASA HEADQUARTERS WASHINGTON, DC	ESTABLISHED POLICY FOR COMMERCIAL USE. MINIMUM BUY IS 1/4 OF PAYLOAD BAY.	10 DAYS
SHUTTLE LAUNCHED SPACECRAFT (UP TO 55,000 LBS.)	ACTIVE	CHESTER LEE CUSTOMER SERVICES NASA HEADQUARTERS WASHINGTON, DC	LAUNCH CAPABILITY DEMONSTRATED. REVISIT CAPABILITY TO BE DEMONSTRATED IN STS-13	6 TO 9 MONTHS

SMALL SELF-CONTAINED EXPERIMENTS

THE PURPOSE OF THIS PROGRAM IS TO MAKE AVAILABLE UNUSED SHUTTLE CARGO BAY SPACE TO SMALL EXPERIMENTS AT LOW COST. THE PROGRAM USES THE CONTAINER APPROACH WHERE SELF-CONTAINED EXPERIMENTS ARE PLACED IN CANNISTERS IN THE SHUTTLE BAY. NASA SUPPLIES THE CANNISTERS AND EXPERIMENT MOUNTING HARDWARE TO THE EXPERIMENTERS. THIS CANNISTER PROVIDES FOR INTERNAL PRESSURE VARIATION AND THERMAL PROTECTION OF EXPERIMENTS. THE SELF-CONTAINED EXPERIMENT CONCEPT PROVIDES FOR VERY LIMITED COMMAND ACCESS TO THE EXPERIMENTS.

THE DIMENSIONS OF THE EXPERIMENTS ARE LIMITED TO VOLUMES OF 5, 2 1/2 OR 1 1/2 CUBIC FEET WITH WEIGHTS OF 200, 100 OR 60 LBS. THE DIAMETER OF THE EXPERIMENT IS LIMITED TO ABOUT 20 INCHES.

ABOUT FOUR-HUNDRED RESERVATIONS HAVE BEEN MADE UNDER THIS PROGRAM TO DATE. SIXTEEN SMALL SELF-CONTAINED EXPERIMENTS HAVE BEEN FLOWN THROUGH 1983 AND FIFTEEN ADDITIONAL EXPERIMENTS ARE SCHEDULED FOR 1984.

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SMALL SELF-CONTAINED EXPERIMENTS

- PURPOSE IS TO MAKE AVAILABLE UNUSED SHUTTLE CARGO BAY SPACE TO SMALL EXPERIMENTERS AT LOW COST
- USES CONTAINER CONCEPT
  - EXPERIMENTS HOUSED IN NASA SUPPLIED CONTAINERS
    - CONTAINER PROVIDES FOR
      - INTERNAL PRESSURE VARIABILITY
      - SOME THERMAL PROTECTION FOR EXPERIMENT APPARATUS
- EXPERIMENTS ARE MOSTLY SELF-CONTAINED
- EXPERIMENT DIMENSION LIMITATIONS
  - VOLUMES OF 5, 2-1/2 AND 1-1/2 CU. FT.
  - WEIGHTS OF 200, 100 AND 60 LBS.
  - DIAMETER LIMITED TO ABOUT 20 INCHES
- SO FAR ABOUT 400 RESERVATIONS HAVE BEEN MADE UNDER THIS PROGRAM
  - 16 FLOWN THROUGH STS-9
  - 15 SCHEDULED FOR 1984

CAPACITY FOR OPPORTUNITY PAYLOAD EXPERIMENTS

THE AIM OF THIS PROGRAM IS TO FILL UNOCCUPIED SHUTTLE CARGO CAPACITY WITH SMALL EXPERIMENTS THAT CAN BE QUICKLY PREPARED FOR A FLIGHT. THE EXPERIMENTS WILL BE CARRIED ON A STRUCTURE THAT SPANS THE WIDTH OF THE CARGO BAY (ABOUT 15 FEET) AND 3 FEET ACROSS. NASA IS ATTEMPTING TO KEEP INTEGRATION COSTS LOW BY USING STANDARDIZED PORTS, FIXED SIGNAL INTERFACES, AND BY OFFERING RESTRICTED ENVELOPES.

THESE PAYLOADS WILL BE MANIFESTED FROM SIX MONTHS TO TWO YEARS BEFORE THE FLIGHT. SINCE INTEGRATION TAKES A MINIMUM OF SIX MONTHS, NO PAYLOAD WILL BE MANIFESTED AFTER THAT TIME. ALSO, NO PAYLOAD WILL BE MANIFESTED TWO YEARS BEFORE A FLIGHT SO THAT LARGER PAYLOADS ARE NOT PREEMPTED.

THIS PROGRAM IS STILL IN THE PLANNING STAGE.

CAPACITY FOR OPPORTUNITY PAYLOAD EXPERIMENTS

- EXPLOITS UNUSED CARGO BAY CAPACITY
  - CARRIER STRUCTURE DIMENSION SPANS THE WIDTH OF THE CARGO BAY AND 1 M ACROSS
  - MAXIMUM LOAD FACTOR OF 25
- CARRIER STRUCTURE WILL HOLD THREE SMALL PAYLOADS OR EXPERIMENTS
- INTEGRATION COSTS KEPT LOW BY
  - USING STANDARDIZED PORTS
  - USING FIXED SIGNAL INTERFACES
  - OFFER RESTRICTED ENVELOPES
- PRICING POLICY
  - STILL BEING WORKED OUT
  - ONE POLICY BEING CONSIDERED CHARGES FOR EXPERIMENT WEIGHT AND VOLUME ONLY
  - COSTS PROJECTED TO BE IN THE $ .5 M - $ 1.5 M RANGE FOR A SMALL EXPERIMENT
- MANIFESTING TIME
  - MINIMUM OF SIX MONTHS-MINIMUM TIME NEEDED FOR INTEGRATION
  - MAXIMUM OF TWO YEARS-DISCOURAGE PREEMPTION OF MAJOR PAYLOADS

SPACELAB SYSTEM

THE SPACELAB SYSTEM CONSISTS OF PALLETS AND MODULES. THE MODULES ARE PRESSURIZED AND HABITABLE. THEY ARE 9 FEET LONG AND 13 FEET IN DIAMETER. WHEN TWO MODULES ARE JOINED, THE CONFIGURATION IS CALLED THE LONG MODULE. THE SINGLE MODULE CONFIGURATION IS CALLED THE SHORT MODULE. THE LONG AND SHORT MODULE CONFIGURATIONS PROVIDE A SHIRT-SLEEVE ENVIRONMENT WHERE THREE MISSION OR PAYLOAD SPECIALISTS CAN WORK ON EXPERIMENTS SIMULTANEOUSLY. THE CONTROL AND THE EXPERIMENT EQUIPMENT IS MOUNTED ON RACKS ALONG THE WALLS OF THESE MODULES.

THE U-SHAPED PALLETS ARE STRUCTURES THAT ARE 13 FEET WIDE, AND 10 FEET LONG. VARIOUS TYPES OF INSTRUMENTS CAN BE MOUNTED ON THE PALLET—UP TO A WEIGHT OF THREE TONS IF LOADED EVENLY. SOME PALLET MOUNTED INSTRUMENTS ARE SELF-CONTAINED OR AUTOMATED. OTHERS CAN BE CONTROLLED FROM THE SPACELAB MODULE ITSELF, THE SHUTTLE AFT DECK, OR FROM THE GROUND. MORE THAN ONE PALLET CAN BE ATTACHED TO ANOTHER TO ACCOMMODATE LARGE EQUIPMENT.

VARIOUS COMBINATIONS OF MODULES AND PALLETS ARE AVAILABLE.

SPACELAB SYSTEM

- COMPOSED OF
  - PALLETS
    - 13 FT. WIDE X 10 FT. LONG CARRIER STRUCTURE
    - CAN ACCOMMODATE UP TO THREE TONS OF EVENLY LOADED EQUIPMENTS
    - EXPERIMENTS CAN BE COMPLETELY SELF-CONTAINED OR CAN BE CONTROLLED FROM SPACELAB MODULE, SHUTTLE AFT DECK, OR FROM GROUND
  - SPACELAB MODULE
    - HABITABLE, PRESSURIZED MODULE - NINE FT. LONG X 13 FT. DIAMETER
    - CONFIGURATION OF ONE MODULE (SHORT MODULE) OR TWO MODULES (LONG MODULE) JOINED TOGETHER
    - EXPERIMENTS ARE IN RACKS IN THE MODULES
- SPACELAB SYSTEM CONFIGURATIONS
  - SHORT MODULE (SM)
  - LONG MODULE (LM)
  - SM + UP TO THREE PALLETS
  - LM + UP TO TWO PALLETS
  - UP TO FIVE PALLETS

TYPICAL TIME LINES FOR USE OF ORBITAL FACILITIES

TYPICAL SCHEDULES FOR THE USE OF THE SPACE SHUTTLE ARE COMPATIBLE WITH THE LEAD TIMES NEEDED FOR THE DEVELOPMENT OF FLIGHT EXPERIMENT EQUIPMENT. FOR EXAMPLE, SMALL SELF-CONTAINED PAYLOADS REQUIRE A LEAD TIME OF ABOUT 18 MONTHS AND SHOULD BE AT THE LAUNCH SITE ABOUT 2 TO 6 MONTHS BEFORE THE SCHEDULED LAUNCH FOR INTEGRATION WITH THE SHUTTLE. LARGER PAYLOADS SUCH AS THOSE INSTALLED IN THE PAYLOAD BAY NEED LONGER LEAD TIMES FOR DEVELOPMENT AND INTEGRATION. EXPERIMENTS WITH COMPLEX INTERFACE AND DESIGN REQUIREMENTS MAY REQUIRE A LEAD TIME OF UP TO THREE YEARS. AS IN THE CASE OF COSTS, NASA CAN BE FLEXIBLE TO ACCOMMODATE THE SCHEDULE REQUIREMENTS OF PRE-COMMERCIAL AND COMMERCIAL FLIGHT EXPERIMENTS.

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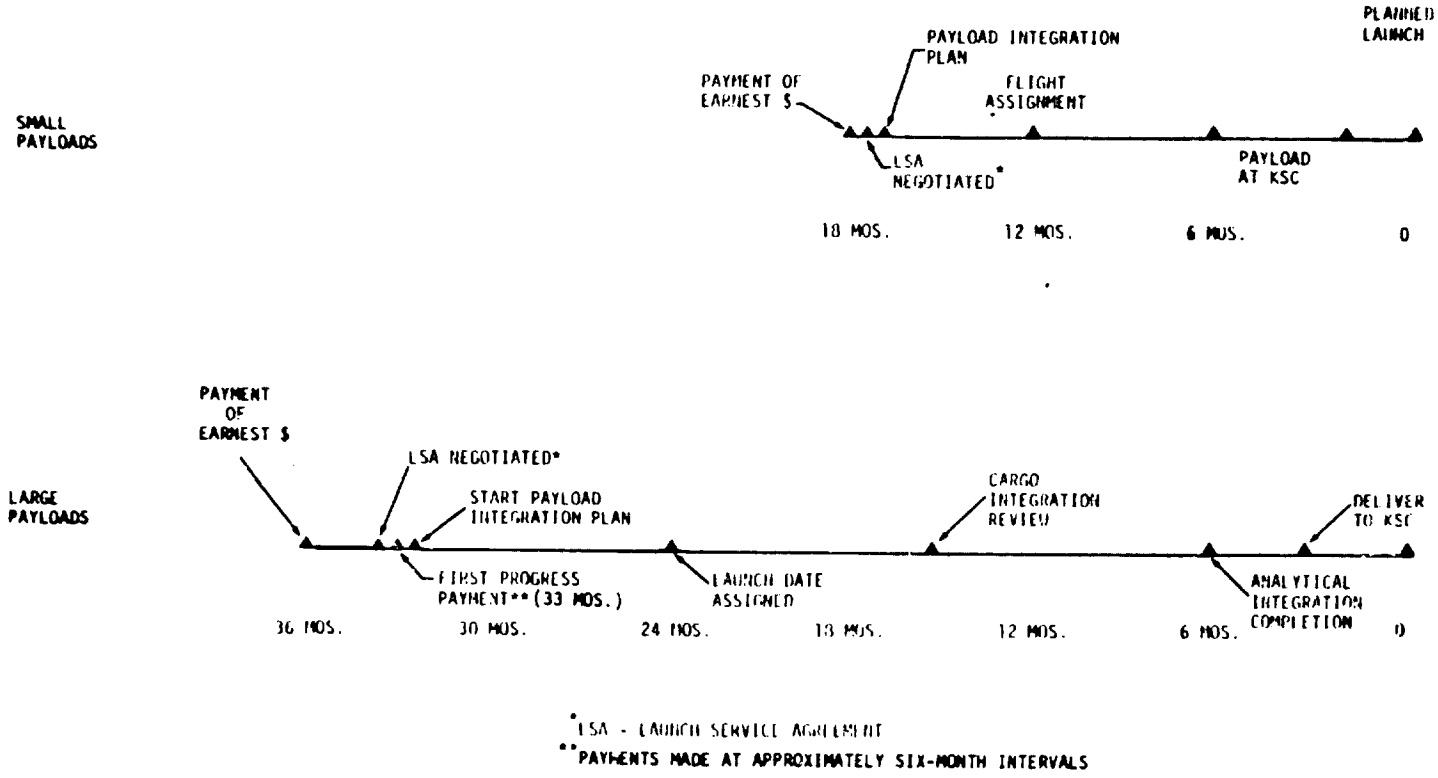
TYPICAL TIME LINES FOR USE OF ORBITAL FACILITIES



*LSA - LAUNCH SERVICE AGREEMENT

**PAYMENTS MADE AT APPROXIMATELY SIX-MONTH INTERVALS

A WIDE RANGE OF POSSIBLE WORKING RELATIONSHIPS

THE NATURE OF THE WORKING RELATIONSHIP POSSIBLE BETWEEN INDUSTRY AND NASA IN THE CONDUCT OF RESEARCH AND DEVELOPMENT IS HIGHLY FLEXIBLE. IT CAN BE DESIGNED TO FIT THE MUTUAL INTERESTS OF BOTH PARTIES. AT THE OUTSET IT IS LIKELY THAT THE ZONE IN THE CENTER OF THE OPPOSITE CHART WILL BE OF MOST INTEREST AS THESE COOPERATIVE ARRANGEMENTS ALLOWS INDUSTRY AND GOVERNMENT TO EACH FOCUS ON AREAS OF THEIR OWN EXPERTISE AND R&D INTERESTS. MOREOVER, THESE COOPERATIVE ARRANGEMENTS ENABLE THE PARTIES TO REDUCE RISK BY THE SHARING OF CERTAIN COSTS SUCH AS SPACE TRANSPORTATION, AND PROVIDE PROTECTION FOR PROPRIETARY RESULTS. UNDER THE AEGIS OF THESE COOPERATIVE AGREEMENTS INDUSTRY AND GOVERNMENT CAN ACHIEVE MUTUALLY SUPPORTIVE ROLES IN SPACE BIO-PROCESSING EXPERIMENTATION AND DEVELOPMENT.

A WIDE RANGE OF POSSIBLE WORKING RELATIONSHIPS

INDUSTRY	• PAY FOR SHUTTLE FLIGHT AND/OR USE OF NASA FACILITIES • PAY FOR AND DEVELOP TEST EQUIPMENT • ALL COSTS PAID BY INDUSTRY • RETAIN FULL DATA RIGHTS	• PAY FOR AND DEVELOP SPECIAL EQUIPMENT SUCH AS TEST EQUIPMENT TO FLY IN SHUTTLE • DATA RIGHTS NEGOTIABLE • PROCESS EXCLUSIVITY	• UNDERTAKE DEVELOPMENT UNDER CONTRACT TO GOVERNMENT
WORKING ARRANGEMENT	COMPANY FUNDED	TECHNICAL EXCHANGE AGREEMENT GUEST INVESTIGATOR JOINT ENDEAVOR AGREEMENT	GOVERNMENT FUNDED CONTRACT
NASA	• INTERFACE, SAFETY, SCHEDULING	• PROVISION OF GOVERNMENT FACILITIES UNDER NEGOTIABLE (NO TO FULL) CONDITIONS OF COST RECOVERY • SOME DATA EXCHANGE AND/OR EXPERIMENTS PERFORMED FOR GOVERNMENT BY CONTRACTOR • INTERFACE, SAFETY AND SCHEDULING	• COMPETITIVE OR UNSOLICITED PROCUREMENT • COULD BE COST SHARED IN RETURN FOR SOME DATA RIGHTS, OTHERWISE DATA RIGHTS BELONG TO GOVERNMENT AND DATA IS IN PUBLIC DOMAIN • ALL COSTS, EXCEPT SHARED, PAID BY GOVERNMENT • INTERFACE, SAFETY AND SCHEDULING

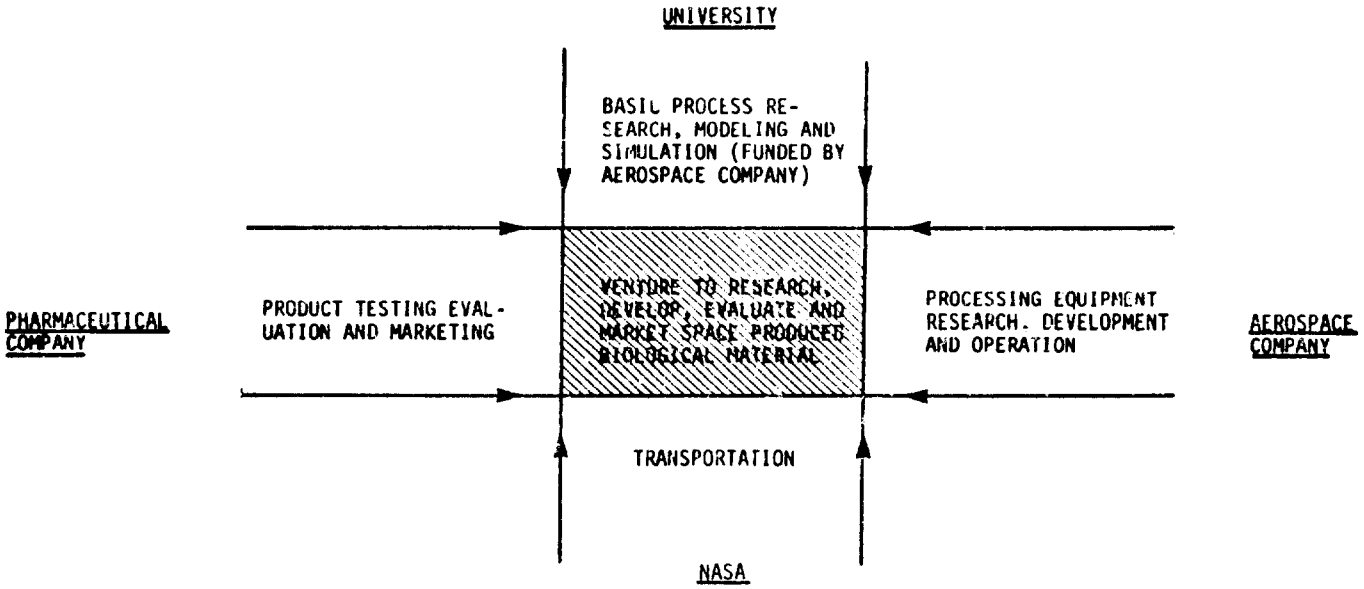
Econ

A MODEL FOR A SPACE BIO-PROCESSING EXPERIMENT

A SPACE BIOPROCESSING EXPERIMENT REQUIRES MANY DIVERSE SKILLS AND CAPABILITIES. THESE INCLUDE THE DESIGN, DEVELOPMENT AND OPERATION OF THE PROCESSING EQUIPMENT; RESEARCH AND DEVELOPMENT NECESSARY TO UNDERSTAND SEPARATION PROCESSES IN THE SPACE ENVIRONMENT; THE TESTING, EVALUATION AND MARKETING OF ANY RESULTANT PRODUCTS; AND THE CAPABILITY TO PLACE INTO ORBIT AND RETRIEVE THE MATERIAL TO BE PROCESSED AND THE PROCESSING EQUIPMENT. AT THE PRESENT TIME IT IS NOT LIKELY THAT THESE CAPABILITIES WILL ALL RESIDE IN A SINGLE ORGANIZATION. THE DESIGN AND DEVELOPMENT OF THE PROCESSING EQUIPMENT REQUIRES AEROSPACE HARDWARE EXPERIENCE. BASIC RESEARCH CAPABILITIES IN COMPLEX FLOW PHENOMENA OF THE TYPE ENCOUNTERED IN ELECTROPHORETIC SEPARATION IS USUALLY FOUND IN A UNIVERSITY ENVIRONMENT. THE ABILITY TO TEST, EVALUATE AND MARKET THE RESULTANT PRODUCT IS A SKILL THAT IS UNIQUE TO THE BIOLOGICAL AND PHARMACEUTICAL INDUSTRIES. NASA HAS DEMONSTRATED THE CAPABILITY TO TRANSPORT BOTH THE PROCESSING EQUIPMENT AND MATERIAL TO AND FROM ORBIT.

THE MODEL AS DESCRIBED IS NOT INTENDED TO BE EXCLUSIVE, AND OTHER COMBINATIONS OF THE NECESSARY RESOURCES ARE POSSIBLE. FOR EXAMPLE, NASA IS SUPPORTING BASIC RESEARCH THAT IS INTENDED TO IMPROVE UNDERSTANDING OF FLOW PHENOMENA IN THE SPACE ENVIRONMENT. MOREOVER, NASA COULD PROVIDE TECHNICAL ASSISTANCE IN THE DESIGN OF THE SPACE PROCESSING EQUIPMENT, OR COULD PROVIDE THE EQUIPMENT FOR EXPERIMENTATION AS A NATIONAL SPACE LABORATORY FACILITY.

A MODEL FOR A SPACE BIO-PROCESSING EXPERIMENT



4. SUMMARY

NASA AND INDUSTRY HAVE CONDUCTED SEVERAL EXPERIMENTS INVOLVING THE USE OF SEPARATIVE TECHNIQUES FOR BIOLOGICAL MATERIALS IN SPACE SINCE 1971. WHILE THE EARLY EXPERIMENTS WERE OFTEN HAMPERED BY EQUIPMENT PROBLEMS THE RESULTS HAVE BEEN GENERALLY ENCOURAGING. THE RESULTS OF RECENT EXPERIMENTS PERFORMED BY MCDONNELL-DOUGLAS AND JOHNSON AND JOHNSON IN THE SPACE SHUTTLE ARE PROPRIETARY; HOWEVER, MCDONNELL-DOUGLAS HAS DESCRIBED THE RESULTS IN VERY POSITIVE TERMS.

NASA HAS BOTH GROUND AND SPACE FACILITIES FOR THE CONDUCT OF MICROGRAVITY RESEARCH. THE GROUND FACILITIES OFFER EXPOSURE DURATIONS RANGING FROM SEVERAL SECONDS TO SEVERAL MINUTES, WHILE THE SPACE SHUTTLE CAN PROVIDE EXPOSURE DURATIONS UP TO TEN DAYS. THE SPACE SHUTTLE HAS THE CAPACITY TO LAUNCH AND RETRIEVE AUTOMATED SPACECRAFT THAT CAN PROVIDE EXPOSURE TO THE SPACE ENVIRONMENT FOR PERIODS OF UP TO SEVERAL MONTHS.

NASA HAS A GREAT DEAL OF FLEXIBILITY IN ESTABLISHING WORKING RELATIONSHIPS WITH INDUSTRY FOR RESEARCH AND DEVELOPMENT INVOLVING THE USE OF THESE FACILITIES. IN PARTICULAR, SHARED COST ACCESS TO THE SPACE SHUTTLE CAN BE NEGOTIATED FOR SPACE BIOPROCESSING RESEARCH AND DEVELOPMENT, AND FLIGHT SPACE CAN BE PROVIDED ON AN ACCELERATED SCHEDULE THAT IS COMPATIBLE WITH THE DEVELOPMENT OF THE EXPERIMENTAL EQUIPMENT.

4. SUMMARY

- EXPERIMENTS INVOLVING THE SEPARATION OF BIOLOGICAL MATERIALS IN THE SPACE ENVIRONMENT HAVE BEEN CONDUCTED BY NASA AND INDUSTRY
  - + FIRST EXPERIMENTS IN 1971
  - + RESULTS HAVE BEEN ENCOURAGING
- NASA CAN PROVIDE BOTH GROUND AND FLIGHT FACILITIES TO SUPPORT EXPERIMENTATION IN A MICROGRAVITY ENVIRONMENT
- NASA IS INTERESTED IN ENCOURAGING EXPERIMENTAL USE OF THE SPACE SHUTTLE BY INDUSTRY AND CAN BE FLEXIBLE IN ESTABLISHING COOPERATIVE WORKING ARRANGEMENTS

Econ

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APPENDIX C

NOTES FROM MEETINGS WITH BIOTECHNOLOGY AND PHARMACEUTICAL COMPANIES

Econ INCORPORATED

INTEROFFICE MEMO

TO: Project File

FROM: B. P. Miller

SUBJECT: Meeting with BioTechnica International, Inc.

DATE: February 6, 1984

1. Details of Contact

Name and Address: BioTechnica International, Inc.
85 Bolton St.
Cambridge, MA 02140

Date : 2 Feb. 1984

Telephone : (617) 864-0040

Contacts : Thomas Coor, Vice Chairman of the Board
Lynn C. Klotz, Vice President, New Product Development
John Marsden, Vice President, Marketing and Sales

2. Background

BioTechnica was selected as a participant in this study on the recommendation of Harvey Price, Industrial Biotechnology Association.

BioTechnica is a young company, 2 1/2 years old. Their scientific staff is drawn mainly from MIT and Harvard. They had a public stock offering in March 1983. Their main areas of business are research and development in the areas of genetic engineering, recombinant DNA and fermentation technologies to develop and produce new strains of microorganisms and altered crop plants. Major areas of business at the present time are the development of advanced microbial production systems for the food, beverage, chemical and pharmacuetical industries, and improvement of plant molecular biology and nitrogen fixation technologies for agricultural applications. Sales in 1983 were "less than $.5 million" and are anticipated to be in the "neighborhood of several million" in 1984. At the present time the company is engaged only in R&D and none of these products have reached the production stage. Their first product will enter the marketplace in 1985, with a second in 1986. Full time staff at present consists of about 65 people, of which 23 hold PhD's.

3. Comments

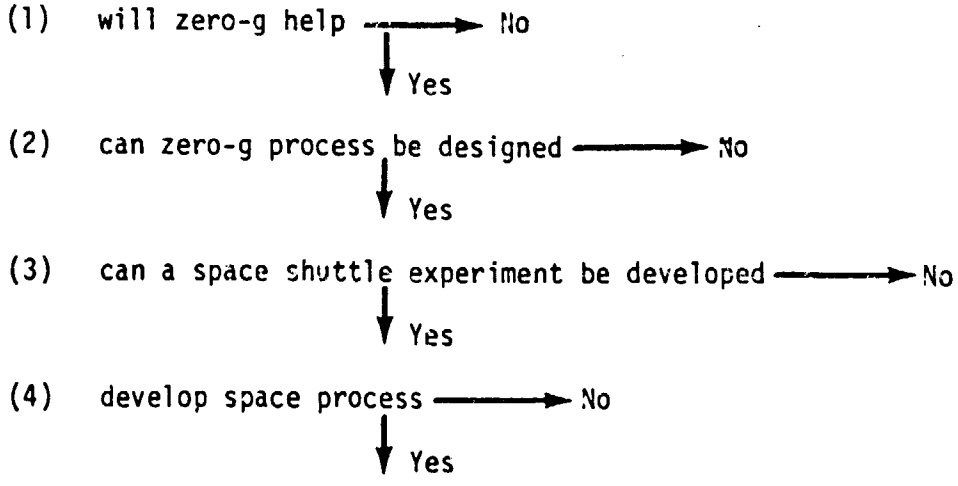
BioTechnica had little prior knowledge concerning the separative experiments conducted by NASA and MDAC. Neither was BioTechnica familiar with

NASA ground research facilities, nor the various possibilities for the use of the Shuttle for experimentation. Moreover, BioTechnica had no prior knowledge of the possibility of cooperative working agreements with NASA.

Dr. Klotz indicated that the free flow electrokinetic separation techniques that have been used by NASA (and appear to be used by MDAC) are indeed bothered by sedimentation and convection effects in a unit-g environment. Because of this, according to Dr. Klotz, other techniques such as gel electrophoresis and density gradient electrophoresis have been developed to get around these problems. These and other laboratory techniques are satisfactory for the production of microgram quantities for analytical purposes. Because of this, Dr. Klotz said that it was his belief that there might only be a narrow window for the use of the zero-g environment. To illustrate this point Dr. Klotz described a simple model for the kind of work performed by BioTechnica:

1.	Bench Scale	R&D	Obtain analytical samples of the product at any cost.
2.	Scale Up	Development	Obtain 10g to 500g samples at acceptable cost and demonstrate feasibility of process or product.
3.	Production		Economic factors dominate.

It was his belief that present laboratory techniques were adequate for the first step and that the use of the space environment might enter at the second or third steps. In our discussion we built the following simple decision tree:



According to Dr. Klotz and Dr. Coor there is feedback from (4) to the preceding steps in terms of the economics. It would be necessary to demonstrate the economic advantage of space processing (an elegant

solution) as opposed to a more brute force approach on the ground. An additional restriction would be the fact that the product must have a high $/mass ratio, otherwise the reasons to use the space environment are not apparent.

4. Actions

BioTechnica would like to obtain the following additional information:

(1) A list, by title of get-away specials with name and affiliation of PI. They are interested in seeing how others are using this low cost mode of experimentation.

(2) More information on the work done by Washington University for MDAC.

(3) Some insight into how they might get MDAC to run samples for Biotechnica in the MDAC CFE device.

Additionally, it was suggested that the development of space processing might be furthered if NASA were to sponsor additional fundamental research in space bioprocessing at the university level and by the presentation of results at international meetings such as Bio-Tech 84 (to be held in Wash., DC, Sept. 1984).

5. Conclusion

This contact had virtually no prior knowledge of the space bioprocessing program or the opportunities for experimentation using the Shuttle. As a result, they were not inclined to think in terms of the use of the space environment. The meeting stimulated their interest and resulted in requests for additional information. However, they remain skeptical about the use of the zero-g environment to make separations economically and competitively with earth-based techniques. The possible use of low cost, self-contained payloads (get-away special) seemed to be of most interest.

ECON INCORPORATED

INTEROFFICE MEMO

TO: Project File

FROM: B. P. Miller

SUBJECT: Meeting with Smith Kline & French Laboratories

DATE: February 10, 1984

1. Details of Contact

Name and Address:		Smith Kline & French Laboratories 1500 Spring Garden St. P.O. Box 7929 Philadelphia, PA 19101
Date	:	6 Feb. 1984
Telephone	:	(215) 751-5500
Contact	:	Dr. George Poste, Vice President, Research and Development

2. Background

Smith Kline was selected as a participant in the study on the basis of the fact that they are a major manufacturer of pharmaceutical, laboratory and medical electronics products. Further, based on information available at the start of the study, Smith Kline is not currently involved with NASA and is not one of the companies that had been contacted by the contractors working for NASA on the space station follow-on activities.

3. Comments

Dr. Poste was knowledgeable about NASA work in space bioprocessing. He said that he derived his information from sources such as the general press, Congressional Testimony and NASA Tech Briefs. He recalled that the President of Smith Kline (Dalby) had been approached by NASA a few years ago in connection with space bioprocessing. He could not recall the details of the contact, but it was clear that there was a residual negative reaction to whatever proposal had been made. Smith Kline had also been approached to sponser a high school science "get-away special." They declined to do so on the basis of the fact that it was their opinion that the proposed high school experiment lacked scientific merit. Smith Kline is not currently involved with NASA at any level, and Dr. Poste did not appear to be aware of the opportunities for cooperative working relationships (i.e. JEA's, etc.) with NASA. According to Dr. Poste, informal discussions had been held at Smith Kline concerning the possible use of the space environment, but that the subject had never been formally considered. Several times during our interview Dr. Poste stated that he believed that the NASA space bioprocessing program suffered from excessive "hype." He cited the President's

budget message, in particular the remarks about using a space station for the production of new drugs as an example of promises that are not based on substance and which are bound to produce a negative reaction in the industry. He said that "the government is ignorant of what industry needs and industry is ignorant of what NASA has to offer."

Dr. Poste then discussed issues relating to the processing of different kinds of biological material in the space environment. The catagories that he mentioned were:

- Pharmaceuticals - micromolecules, molecules, marcromoloecules or cells
- Diagnostics and biosensors

He said that there were many factors that worked against the use of the space environment for the processing of pharmaceutical materials. First was the issue of cost. According to Dr. Poste, the additional increment of R&D cost associated with the use of space might make the product not economically feasible. Dr. Poste said that scale, or the ability to produce the material in sufficient quantity, was also a major factor against the use of the space environment for processing pharmaceuticals. He said that the evaluation of a product for acute therapy (for reasons of therapy, safety, formulation,bioavailability and storage) might require several hundred kilos of material. Other issues that were raised by Dr. Poste included the timetable (long lead time) for delivery of payloads prior to launch and the lack of special handling facilities for biomedical payloads prior to launch and upon immediate return from orbit. He voiced two concerns; namely, the production of this quantity of material in the space environment and the cost of producing this quantity.

Space could be important in the preparation of diagnostic and biosensor analysis materials. Their applications require smaller quantities of high $/mass ratio enzymes that could conceivably be manufactured economically in space.

He stated that electrokinetic separation techniques are not that important to the classes of materials that are used by Smith Kline, and that affinity chromotography separation solves the convection and sedimentation problems seen in electrokinetic separative technicques. Affinity chromotography can be scaled up.

4. Actions

Dr. Poste would like to obtain additional information on "get-away specials." He would like to have a list of experiments, abstracts and PI identification. He would also like to be kept aware of scientific progress in space bioprocessing.

5. Conclusion

This contact was pretty much up to speed on what has been done to date in space bioprocessing, but was not knowledgeable about the possibility of cooperative working arrangements with NASA. His discussion with me projected a degree of professional conservatism concerning the use of the

space environment and a negative reaction to some of the PR concerning the possible benefits of the space environment to the pharmaceutical industry. The thought of the possibility of conducting R&D on a small scale through the "get-away special" seemed to be attractive to Dr. Poste, although his interest here may be aimed at getting up to speed on the scientific use that is being made of the "get-away specials."

Econ INCORPORATED

INTEROFFICE MEMO

TO: Project File

FROM: B. P. Miller

SUBJECT: Meeting with Damon Biotech

DATE: February 13, 1984

1. DETAILS OF CONTACT

Name and Address:	Damon Biotech, Inc. 119 Fourth Avenue Needham Heights, MA 92194
Date:	9 February 1984
Telephone:	(617) 449-6002
Contacts:	Dr. R. Dana Ono, Manager, Technology Resources Dr. Brandon Price, Product Director, Cell Products Ms. Marcia Amsterdam, Vice President, Public Information

2. COMMENTS

Damon Biotech was selected as a participant in this study on the recommendation of Harvey Price of the Industrial Biotechnology Association.

Damon Biotech is a subsidiary of the Damon Corporation that went public in 1983 and raised about $\$40 \times 10^6$ through a public issue. Damon Biotech is still about 70% owned by the Damon Corporation.

Damon Biotech has developed a proprietary technique called ENCAPCEL that facilitates the high density growth of cells and gives product yields as much as 1,000 times greater than other methods. ENCAPCEL is being used to manufacture production quantities of monoclonal antibodies such as Interferon. Damon Biotech has entered into a joint development agreement with the National Cancer Institute to conduct clinical trials of cancer treatments using ENCAPCEL. The first test involves the use of monoclonal antibodies in the treatment of B-cell lymphomia cancer.

The agreement with the National Cancer Institute was announced 19 October 1983. In addition, Damon Biotech is conducting animal studies of the use of ENCAPCEL for the treatment of diabetes. In this case, healthy pancreatic cells are encapsulated and are transplanted to a diabetic host. The healthy cells then act as a self adjusting insulin source.

Market applications of current interest to Damon Biotech are listed below:

Market	Antibody Function	Applications	Quantity of Antibody Needed
Therapeutic	Destruction of diseased cells	B-cell Lymphoma T-cell Lymphoma Colon cancer Autoimmume diseases	
	Immunosuppression	Organ transplantation	Kilograms per product
	Drug targeting	Cancer therapy Antibiotic delivery	
	In vivo neutralization of toxins	Bacterial toxins Chronic viral infections	
Industrial Purification	Separation of product from contaminants	Protein purification (e.g., interferon, growth hormone	Kilograms per product
Diagnostic Imaging	Diagnosis of disease by specific monoclonal antibody coupled to radioisotopes or non-isotopic markers	Diagnosis of tumors Evaluation of tumor chemotherapy Assessment of heart damage	Kilograms per product
Laboratory Diagnostics	Improved specificity of immunodiagnostic kits	All immunodiagnostic kits including cancer, infectious diseases, hormone levels	Grams to kilograms per product

Source: Damon Biotech Annual Report 1983

At the present time, Damon Biotech has a staff of about seventy people. They are constructing the world's largest monoclonal antibody facility that will come on line in May 1984. At the present time, it appears that Damon Biotech uses the ENCAPCEL technique to produce products for other companies (i.e., Interferon for Hoffman LaRoche). According to Dr. Ono, they are working on other products using the same technique for the treatment of diabetes and cancer, as well as for the controlled release of pharmaceutical materials.

3. COMMENTS

Dr. Ono and Dr. Price said that they were both very interested in space bioprocessing, but that they knew very little about the NASA program. They indicated that their main sources of information were the general press. Dr. Price said that he had a classmate at JPL and that he often called his classmate when he had questions about the space program. Neither Dr. Ono nor Dr. Price were aware of the possibility of engaging in a cooperative R&D program with NASA.

Following our discussion of the NASA program, I was told that Damon Biotech could use additional information on the scientific aspects of the NASA program. Specific requests were made for information about the "get away special" experiments, and concerning any work that NASA might have done on the productivity and fusion frequency of hybridomas in zero g. I was asked if it was possible for NASA to provide a speaker well versed in the science aspects of the space bioprocessing program to talk to their Scientific Board consisting of top level research scientists from MIT and Harvard.

Possible applications of the space environment that were suggested in our meeting included the investigation of cell efficiency (productivity and fusion frequency) in the zero g environment and the use of electrophonesis to separate contaminants from monoclonal materials. Cell efficiency seemed to be of major interest, and Dr. Ono indicated that if the absence of gravity improved efficiency, it might be possible to produce very valuable products in small scale facilities.

Dr. Ono mentioned that he had brought up the possibility of using the space environment at a staff meeting and that the comments were favorable. However, their resources did not permit them to move in the direction of space research at that time. I was told that the people at Damon Biotech need more information on how to do business with NASA. "Where is the bridge between NASA and the biotechnology companies?"

4. ACTIONS

(1) Provide a speaker who can talk knowledgeably about the science aspects of the NASA space bioprocessing program to meet with their Science Board.

(2) Follow up our question concerning any NASA research on the effects of zero g on cell efficiency.

(3) Provide information on use of "get away specials" including titles, abstracts, and Principal Investigator identification.

(4) What is MDAC posture on processing material supplied by Damon Biotech in their electrophonesis experiments in the Shuttle? What would it cost?

5. CONCLUSIONS

Dr. Ono and Dr. Price appeared to be interested in exploring how Damon Biotech might use the space environment. There is a need to supply them with additional information and to follow up on the actions noted above. Neither of the participants in the meeting appeared to have much prior knowledge concerning the NASA program or the possibility of engaging in a cooperative R&D effort with NASA.

BPM:nw

Econ INCORPORATED

INTEROFFICE MEMO

TO: Project File

FROM: B. P. Miller

SUBJECT: Meeting with E. R. Squibb

DATE: February 13, 1984

1. DETAILS OF CONTACT

Name and Address:	E. R. Squibb P. O. Box 400 Princeton, NJ 08540
Date:	TO February 1984
Telephone:	(609) 921-4000
Contacts:	Dr. Zola Horovitz, Vice President, Research and Development (Squibb)* Dr. Grant Gibbons, Product Development and Planning Manager (Squibb) Mr. Hank Bauer, Director, Manufacturing Operations (Squibb) Mr. Glenn A. Brewer, Assistant Director, Analytical Research (Squibb) Dr. Klaus Florey, Director, Analytical and Physico-Chemical Research, (Squibb Institute for Medical Research) Dr. George B. Mackaness, President (Squibb Institute for Medical Research) Mr. J. D. Pipkin, Senior Research Scientist, Pharmaceutical Research and Development (Squibb) Mr. Mike Varia, Director, Strategic Planning (Squibb)

2. BACKGROUND

Squibb was selected as a participant in this study on the basis of the fact that they are a major international manufacturer of pharmaceutical products, with subsidiaries with product lines in laboratory

*Principal Contact

and medical electronics. Further, based on information available at the start of this study, Squibb was not involved with NASA and is not one of the companies that has been contacted by the contractors working on the Space Station follow-up activities.

3. COMMENTS

In addition to the author of this report, Dr. Edwin Dupnick of ECON and Ms. Helene Najduk of NASA also participated in this meeting.

It was clear from the meeting that Squibb had little prior knowledge about the work that had and is currently being performed by NASA in the field of space bioprocessing. Nor did the participants in the meeting have prior knowledge about the possibility of establishing cooperative arrangements with NASA (such as a JEA). It was indicated that perhaps two or three years ago Squibb had undertaken a contract for NASA in support of an RTG development, but that work was outside of the pharmaceutical area.

Their initial reaction to our presentation was to ask how they could obtain additional information on past and planned space bioprocessing that is being performed for NASA. We were asked about the availability of scientific reports, abstracts, and bibliographies covering the work performed by NASA and its contractors. We were asked if NASA could provide a speaker to talk to senior management of Squibb about the scientific results of experiments conducted to date and about the scientific goals of future planned space bioprocessing experiments. In subsequent discussion, we were told by Squibb (Dr. Horovitz) that two types of meetings might be worthwhile; the first for a small meeting of high level scientific personnel, and the second for a large meeting of Squibb middle management. We were further asked if NASA could make available to Squibb an index or database of literature that has been published on the scientific and technical aspects of space bioprocessing. When I showed one of the participants a paper that had been published by the American Astronautical Society on an electrophoresis experiment in STS-3, we were told that publications that deal with astronautics are not usually read by people in the pharmaceutical field.* It was suggested that articles of this sort might better be published in Science or Nature. One of the participants had the notice for the forthcoming AIAA sponsored meeting on space bioprocessing in Houston that he had received from the Pharmaceutical Manufacturers Association.**

*Electrophoretic Purification of Cells in Space: Evaluation of Results from STS-3, Burton E. Sarnoff, M. Elaine Kunze, and Paul Todd. American Astronautical Society, 83-212.

**Space Bioprocessing Seminar, 7, 8 March 1984.

It was suggested that NASA publish more in journals that the pharmaceutical industry normally uses, and that more meetings of the sort planned for Houston should be held.

With the exception of diagnostic materials, the products made by Squibb are usually produced in large volume, i.e., tons of material. The participants in the meeting found it difficult to visualize how a plant that could produce tons of pharmaceutical materials per year could be made economic in the space environment. For example, it was said that Squibb had just spent the cost of one shuttle flight (i.e., about $\$70 \times 10^6$) to build a production facility that would hopefully last forty years. I responded that within a decade it may be possible to build a plant in space that would last forty years; however, the high cost of transporting large volumes of material to and from space was recognized as a deterent to large volume production in the space environment.

Several of the Squibb people present suggested that the zero g attribute of space was of interest to them for R&D purposes. For example, it was suggested that it might be possible to separate a cell population in space that is difficult to separate on earth. The separated cells could be brought back to earth and then replicated. This concept might be applicable for diagnostic materials. It was also suggested that the improvement obtained by conducting separations in the space environment might be a possible service business. In this case, the operator of the separative equipment in space could sell services to pharmaceutical companies for purposes such as determining the purity of a new drug, identifying small (.01%) impurities, or producing analytical or preparative quantities of a material. The radiation and cryogenic temperature attributes of the space environment did not elicit much interest, although one of the Squibb participants asked if NASA had conducted freeze drying experiments in the space environment.

It was pointed out that from their perspective, commercialization means large volume production, not simply the use of space for commercial purposes. It was difficult for them to postulate on how they might use the space environment since they had not had much prior information, nor was the use of the zero g environment something that they routinely thought about. Given their present state of knowledge, it was clear that the use of space would be considered only if there was no other way to accomplish what had to be done.

4. ACTIONS

(1) Provide a speaker well versed in the science aspects of the space bioprocessing program to talk to a small group of senior scientific people at Squibb.

(2) Provide a more general engineering oriented speaker to talk to a large meeting of Squibb middle management at a Management Club dinner meeting.

(3) Provide an index and/or database of publications on space bioprocessing.

(4) Provide data on the experimental use of the "get away special" experiments such as titles, abstracts, names, and affiliation of Principal Investigators.

(5) Provide data on NASA owned space bioprocessing equipment that might be available for experimental use by Squibb in the shuttle program.

5. CONCLUSIONS

We met with a large group of senior R&D and R&D management personnel. It was clear that they knew little about the NASA space bioprocessing program, nor did they have any prior knowledge about the possibility of cooperative working relationships (JEA) with NASA. In fact, one of the Squibb participants stated that their normal method of obtaining information on NASA programs would be to query the IAC at the University of Pittsburgh. Although no specific experiments were suggested, there seemed to be a strong interest on the part of the Squibb participants in obtaining follow-up data that might help them better understand how they might use the space environment.

BPM:nw

Econ INCORPORATED

INTEROFFICE MEMO

TO: Project File

FROM: B. P. Miller

SUBJECT: Meeting with Merck, Sharp and Dohm

DATE: March 2, 1984

1. DETAILS OF CONTRACT

Name and Address:	Merck, Sharp and Dohm Research Laboratories Division of Merck & Co., Inc. P.O. Box 2000 Rahway, NJ 07065
Date:	17 February, 1984
Telephone:	(201) 574-6447
Contacts:	Mr. James Lago, Vice President for Development and Process Chemistry Dr. Lewis Mandel, Senior Director, University/ Industry Relations In addition to the above, Ms. Helene Najduk of NASA Headquarters also participated in this meeting.

2. BACKGROUND

Merck was selected as a participant in the study on the basis of the fact that they are a major manufacturer of pharmaceutical products. Moreover, at the time of their selection, it was believed that Merck was not involved with NASA and is not one of the companies that has been contacted by the contractors working for NASA on the space station follow-on activities.

3. COMMENTS

Mr. Lago had heard a presentation by MDAC at a SNOWMASS meeting several years ago and Merck had also participated in a study group with Rockwell. The attitude that was projected is that Merck has been involved and is up to speed on the subject of space bioprocessing. Mr. Lago indicated that space bioprocessing has been discussed within Merck but that they have not been able to come up with anything that looks like an economically feasible process.

Mr. Lago stated that he was not sanguine about the use of electrophoresis in space as a general purpose separation technique of commercial significance. For most applications, there are more economic methods available. He indicated that separation methodologies have increased in number and in effectiveness in recent years. Further, advances in biotechnology have simplified separation problems through the ability to preferentially produce desired biological molecules as well as by providing powerful separation techniques. Procedures now in use in their laboratories are adequate for current projects. Mr. Lago said that Merck has a research and development staff of about 3,000 people and that the individual scientists follow the literature in their own areas of interest. No specific attempt is made to obtain NASA publications and no specific individual is responsible for following the activities of NASA in space bioprocessing. Dr. Mandel pointed out that Merck probably does not get aerospace journals and would not see the result of NASA work unless it was published outside of such journals. There was interest on the part of Merck in receiving additional scientific information, information about experiments performed to date by NASA and others or characteristics of available equipment that could be used, but more for background information than for problems needing solution. In response to a specific question, Mr. Lago said that at this time Merck has no separation problems that would be benefited by electrophoretic processing in a micro gravity environment and therefore would not be interested in using NASA or MDAC separative equipment to process samples furnished by Merck.

4. ACTIONS

None.

5. CONCLUSIONS

There is little interest at Merck at the present time in space processing because no benefit is seen for current research and development programs. The open literature is followed, and if opportunities not now envisioned develop, the interest would increase.

ECON INCORPORATED

INTEROFFICE MEMO

TO: Project File

FROM: B.P. Miller

SUBJECT: Meeting with Upjohn

DATE: March 6, 1984

1. DETAILS OF CONTACT

Name and Address:	The Upjohn Company 7000 Portage Road Kalamazoo, MI 49001
Date:	February 22, 1984
Telephone:	(616) 323-4000
Contact:	Dr. Jacob Stucki, Vice President Pharmaceutical Research and Development

2. BACKGROUND

Upjohn was selected as a participant in this study because they are a major U.S. developer and manufacturer of pharmaceuticals. Additionally, Dr. Stucki is Vice Chairman of the Pharmaceutical Manufacturers Research Association and Development Steering Committee. Our contact at the PMA, Mr. Chuck Cleveland, further indicated that Dr. Stucki would be a good person to talk to in this study.

3. COMMENTS

Dr. Stucki has given testimony to Congress on behalf of the proposal to establish (and fund at the outset with NASA money) a university research and development center that specializes in zero gravity bioprocessing. Dr. Stucki said that he was familiar with the MDAC work in continuous flow electrophoresis, and that he had attended a PMA meeting where someone from MDAC had conducted a briefing on their work (I believe that this was the PMA R&D Annual Meeting on April 27-30, 1983. Presentations were made by Mr. Joseph Coleman of MDAC and Mr. Louis Hemmerdinger of Grumman at this meeting).

Dr. Stucki indicated that he had a strong personal interest in space bioprocessing and that he had an intuitive belief that it could offer a new way to get some interesting things. However, he added that space bioprocessing was not a basic goal for Upjohn, and that its value to Upjohn would depend upon the problem that they were trying to solve.

As an example of the potential value of space bioprocessing, Dr. Stucki mentioned a cell cycle experiment that he believed was planned for the Shuttle in 1986. The purpose of the experiment is to examine the effects of cell cycle inhibitors on cell performance. He seemed to recall that the PI is an Astronaut who is also an onocologist.

He indicated that he had been instrumental in getting Dr. Alan J. Parcells to participate in the March 1984 NASA/AIAA space bioprocessing meeting in Houston, TX. He felt that the involvement of Parcells was appropriate because Parcells was involved in the development of pilot plant processes to produce preparative quantities of interesting materials that Stucki identifies in the laboratory. Dr. Stucki said that his laboratory people can figure out ways to get analytical quantities (milligrams to grams) of almost anything, but that this statement could not be made about larger quantities (preparative quantities).

According to Dr. Stucki, the J&J involvement with MDAC is an aberation and not typical of what could be expected from the pharmaceutical industry. J&J is much more diversified than most pharmaceutical companies and is made up of many small cost centers. Upjohn is a more typical pharmaceutical company, and in Upjohn the driving factor is to find chemical entities that have potential market value. There was some speculation on his part concerning how J&J got involved with MDAC. He suggested that it might have happened because of fortuitous contact between top level executives in the two companies. In this connection, Dr. Stucki mentioned that someone from NASA had approached their President but that Upjohn did not see anything of interest in the NASA proposal.

Dr. Stucki pointed out that from the viewpoint of the pharmaceutical industry, what MDAC and NASA had to offer was a means to an end, but not the end itself. As far as Dr. Stucki was concerned the end was the chemical or biological entity. He viewed the space industry as driven by a desire to sell space technology, while the pharmaceutical industry is driven by the need to find new marketable products. He indicated that as a process, the separative work that is typified by the MDAC effort must fit in as a process into either (1) new entity identification or (2) new entity product. It was his view that the separative technology was probabaly of greater interest to production.

Dr. Stucki indicated that cell cycle performance and the growth of protein crystals were two interesting areas of possible investigation for space

bioprocessing. He said that separative technology could also be interesting for the production of analytical quantities in space if the device used could yield improved resolution. However, it was his perception that the resolution of the MDAC device was not very good. I pointed out to him that NASA was developing an isoelectric focusing machine (Dr. Bier, Univeristy of Arizona) and that the Bier machine was said to have improved resolution.

He said that the best way that he could think of to advance the NASA program was to get technical data on the NASA work and capabilities in front of their laboratory people so that their people would begin to view space as an alternative for either R&D or production. He specifically suggested that it would be useful to have information on space bioprocessing devices at the annual Pittsburgh instrument manufacturers meeting and technical exhibit. He stressed the fact that the pull for the use of space bioprocessing had to come from their middle level managers and researchers - not from him, and that these people needed additional information if they are to consider space as an alternative.

Hasn't Marshall been working w/ Upjohn?

4. ACTIONS

(1) What are the expected or measured operating characteristics of the isoelective focusing device that has been developed by Dr. Bier at the University of Arizona?
(2) Make available technical information on space bioprocessing experiments in a form that can be easily accessed by laboratory R&D personnel.

5. CONCLUSION

Dr. Stucki has had more prior contact with the space bioprocessing program than any of the other contacts made in this study. Although he was not able to identify any specific applications for space bioprocessing within Upjohn, he has a strong belief that the NASA program is valuable and of potential benefit to the pharmaceutical industry. Particular applications that were suggested were protein crystal classification, isolation of new substances of interest and production of preparative quantities.

Econ INCORPORATED

INTEROFFICE MEMO

TO: Project File

FROM: B.P. Miller

SUBJECT: Meeting with Genex Corporation

DATE: March 8, 1984

1. DETAILS OF CONTACT

Name and Address:	Genex Corporation 16020 Industrial Drive Gaithersburg, MD 20877
Date:	February 24, 1984
Telephone:	(301) 258-0552
Contact:	Dr. Kevin Ulmer, Vice President Advanced Technology

2. BACKGROUND

Genex was selected as a participant in this study on the basis of the recommendation of Harvey Price, Industrial Biotechnology Association.

Genex was established in 1977 and had a gross revenue of $5,203,193 in 1982, with total assets of about $32 million. The major emphasis of the company has been the development of proprietary products for food processing, industrial and commercial applications. The commercial strategy of Genex has not emphasized pharmaceutical products because of the extensive testing requirements and the regulatory delays that are involved in bringing pharmaceutical products to the market. However, Genex does engage in contract research and development of various pharmaceutical products including therapeutic enzymes and therapeutic proteins.

3. COMMENTS

Kevin Ulmer had a good background of knowledge on the space program. While he was a graduate student at MIT he applied to be a Mission Specialist on the Shuttle. He is a member of the L-5 Society. He has had discussions with Dr. Gerald Soffen, formerly the Director of the Life Sciences Division of NASA Headquarters, on space processing.

According to Dr. Ulmer, Genex has decided not to become a pharmaceutical company. He said that only one new pharmaceutical company has come into being since World War II, namely Syntex. The FDA requirements for clinical trials and testing are too much of an obstacle for new entries. For this reason, Genex has stayed away from regulated products and has concentrated their efforts on higher volume (lower unit value) production products. However, Genex has cloned products such as interferon and urokinase under contract to pharmaceutical companies. Dr. Ulmer commented that the separation and purification experiments that are being conducted by NASA and MDAC in the space shuttle have largely been obsoleted by recombinant DNA technology and genetic engineering. It was his opinion that electrokinetic separation in zero g might be useful for a few kinds of materials such as living cells, but it was his opinion that the NASA research in electrokinetic separation has not caught up with the new technologies of genetic engineering.

He suggested that protein crystalography might be a productive area for R&D. He indicated that there were three aspects that are important in protein crystalography:

(1) Quantity
(2) Purity
(3) Size

Problems of quantity and purity can be solved on the ground. The space environment may be helpful in the growing of crystals of sufficient size. At the present time the characterization of crystals by x-ray crystalography is limited by the fact that only a small number of proteins can be grown into crystals that are large enough. Most protein crystals are smaller than 1 millimeter and sizes larger than 1 millimeter are needed for many experiments. Dr. Ulmer suggested that since larger crystals of inorganic materials could be grown in space than on the ground, it should be possible to grow larger crystals of proteins in space than on the ground. If the crystals could survive the mechanical environment of the return trip they could be characterized on the ground. If the mechanical environment was too severe and caused the crystals to fracture, it would be necessary to perform the x-ray crystalography in space. Dr. Ulmer suggested that there would be a market for the crystals grown in space in a manner similar to the monodispersed polystryrene latex spheres that were grown in an earlier shuttle flight.

Dr. Ulmer suggested that it would be necessary for aerospace companies to take a much more aggressive posture with the biotechnology and pharmaceutical companies if the goal was to involve more of these companies in space R&D. The biotechnology companies are innovative but do not have much money, while the pharmaceutical companies have money but are not very innovative.

Dr. Ulmer described a center for Advanced Research and Biotechnology that is being established by NBS and the Univeristy of Maryland in Gaithersburg. Montgomery County will provide the land and $5 million for a facility. The

State of Maryland may also provide funds. Several pharmaceutical companies including one of the larger Japanese pharmaceutical companies (Otsuka) have expressed an interest in participating. The Center would provide the opportunity for collaborative or proprietary R&D. The key person at the University of Maryland is Dr. Rita Colwell, Vice President for Academic Affairs (853-6000)

4. ACTIONS

Dr. Ulmer asked the following specific questions:

(1) Can we provide some examples of the cost of development of get away special experiments?

(2) What other (other than MDAC) aerospace companies are capable and/or interested developing hardware for space bioprocessing?

(3) What hardware is currently available that might be used for space bioprocessing experiments?

(4) Can we furnish some specific scientific references to work that has been done or is planned for space in the area of protein crystal growth?

5. CONCLUSION

Dr. Ulmer was knowledgable concerning the NASA space bioprocessing program and outspoken about the fact that the current emphasis on separative R&D was misplaced. He expressed an interest in obtaining additional information concerning the possibility of using the space environment for R&D in protein crystal growth.

Econ INCORPORATED

INTEROFFICE MEMO

TO: Project File

FROM: B.P. Miller

SUBJECT: Meeting with Biogen Research Corporation

DATE: March 9, 1984

1. DETAILS OF CONTACT

Name and Address:	Biogen, Inc. 14 Cambridge Center Cambridge, MA 02142
Date:	February 27, 1984
Telephone:	(617) 864-8900
Contacts:	Richard Aldrich, Business Analyst John Smart, Associate Research Director, Head of Protein Chemistry Wm.S. Kelley, Vice President for Research Administration

2. BACKGROUND

Biogen was selected as a participant in this study on the basis of the recommendation of ~~Mr. Harvey Price~~ of the Industrial Biotechnology Association. Biogen is a Swiss company and the Cambridge, MA facility is headquarters for its U.S. operations.

Biogen was just granted an European patent for genetically manufactured alpha interferon. Their U.S. patent application for alpha interferon is pending. Biogen has licensed Schering-Plough to market the alpha interferon in Europe under the trade name of Intron. Their major competition is Hoffman-La Roche which is testing an interferon product made by Genetech.

3. COMMENTS

Dr. Smart began by saying that Biogen uses electrokinetic separation of the type that is being explored in the Space Shuttle to obtain analytical quantities of substances of interest. Once the substance of interest has been obtained, preparative quantities are obtained using genetic engineering techniques. In general Biogen lacks the financial capability to put large sums of money into the development of new separation techniques and equipment.

They also do not have the technical background to develop space qualified equipment. However, Biogen might be interested in participating in separation experiments in space if they could use an existing device and did not have to build their own separation equipment. The example given by Dr. Smart was a case where Biogen might provide a sample for separation. The sample would be resolved into five or six separate proteins of interest, and returned to Biogen. Biogen would then use the separated materials either as the basis for replication using genetic engineering techniques, or would use the sample to obtain structural data on the protein of interest. In the latter case, x-ray crystalography would be used to characterize the protein.

It was suggested that the space environment might be useful to grow protein crystals for x-ray crystalography, or tc separate specific cell populations. The latter would require finer resolution than can be obtained on earth. In the case of crystal growth, the crystals might be used to verify the lot quality control by crystal uniformity. It was emphasized that the latter application was not a requirement at the present time and that Biogen was debating the issue of lot verification with the FDA.

Dr. Kelley pointed out that their main source of information about space bioprocessing is the Boston Globe (newspaper), and that an easily accessible database that contains scientific information on space bioprocessing experiments would be of great value. It was also indicated that Biogen would be interested in talking to knowledgeable people from the scientific side of the NASA space bioprocessing program.

4. ACTIONS

(1) Can NASA provide a database that covers the science aspects of work that has been done or is planned in the area of space bioprocessing?

(2) Can NASA scientists be made available to talk to their scientific people about the NASA program?

(3) Can information concerning NASA work on sensitive films, filters, cameras and digital image processing be made available to Biogen?

Don't follow-up unless they team up w/ U.S. firm & bal. of benefits flows to U.S.

5. CONCLUSION

Biogen had little previous information concerning either space bioprocessing or the opportunities for collaborative R&D with NASA. Possible applications of protein crystal growth and cell separation were suggested as being of interest, particularly if it was possible for Biogen to use an existing experimental apparatus (or if Biogen did not have to pay for the development of the experimental device). Specific requests were made for follow-up information on the science aspects of the NASA space bioprocessing program.

Econ INCORPORATED

INTEROFFICE MEMO

TO: Project File

FROM: B.P. Miller

SUBJECT: Meeting with Sepracor, Inc.

DATE: March 21, 1984

1. DETAILS OF CONTACT

Name and Address:	Sepracor, Inc. 1101 State Road, Bldg. 0 Princeton, NJ 08540
Date:	March 13, 1984
Telephone:	(609) 924-3022
Contact:	Timothy J. Barberich, President and Chief Executive Officer

2. BACKGROUND

Sepracor was selected as a participant in the study because they are a start-up biotechnology company that will specialize in separation technology. Sepracor was founded by Robert F. Johnston Assoc. Robert Johnston is the founder of both Genex and Cytogen. Sepracor is in the very early stage of formation. At the present time Mr. Barberich is preparing a business development plan that Sepracor will take to the venture capital community to raise seed money for the company.

3. COMMENTS

Sepracor will provide biological separation services to the pharmaceutical and other biothechnology industries. Sepracor will be based upon membrane and chromatography technology. Both membrane and chromatography are used in separations at the present time. Their concept is what Mr. Barberich called an active membrane and involves using a membrane that is 100μ thick and thousands of square feet in area.

Mr. Barberich indiated that his knowledge of NASA work in space bioprocessing was obtained from newspapers and TV. He was not aware of the opportunities for cooperative R&D with NASA. He was aware of the NASA/MDAC/J&J activity and characterized it as "a solution looking for a problem".

He said that Sepracor as a pre-startup company was not in a position to undertake cooperative R&D with NASA because of the lack of capital. If Sepracor was a more mature company with financial reserves available, he would be interested in exploring several possible areas of R&D concerning the effects of micro gravity or separation processes.

The areas suggested were:

(1) Magnetic Separation.

Magnetic separation techniques are being explored in university research and are not commercially available at the present time. Magnetic separation involves the use of a colliodal suspension of magnetic particles to which antibodies have been attached. The magnetic particles surround the cells of interest and subsets of cells can be separated on the basis of their magnetic properties. Mr. Barberich suggested that connective forces might limit the use of this approach in a unit-g environment in a manner that is similar to the limitations imposed on electrokinetic separation. He contrasted magnetic separation to the present techniques used in biotechnology of attaching the ligand to a solid and then using filtration for separation. In magnetic separation the ligand would be attracted to a particle in suspension and magnetic separation would be used to isolate subsets of cells of interest. This would produce what Mr. Barberich called magnetic immunsorbants.

(2) Behavior of Immobilized Enzymes in Zero-G.

Enzymes are proteins that serve a catalytic function in a biotechnology reaction. The enzymes are separated from the reaction broth and are reused. He suggested that the reaction might be enhanced by zero-G. If the turnover rate is higher it might be possible to get the same output with a smaller reactor.

In addition to the foregoing Mr. Barberich said that his company was looking for technologies that might be useful for biological separation processes. He asked if it might be possible for him to obtain access to a database that describes NASA work in this area. Sepracor would be interested in exploring the possibility of licencing NASA technologies that might be useful in their work. Mr. Barberich also expressed an interest in obtaining information on NASA space bioprocessing work in areas that might be applicable to his interests, and in the availability of NASA hardware that might be used for coopeative experiments.

4. ACTIONS

(1) Provide a database of NASA space bioprocessing experiments, and in particular, any experiment that might deal with membranes or magnetic separation.
(2) Provide a database of hardware that might be available from NASA for cooperative experiments.
(3) Put Mr. Barberich in contact with NASA Technology Utilization to discuss NASA biological separation that might be licenced to Sepracor.

OK

5. CONCLUSION

Mr. Barberich had little prior knowledge about the NASA space bioprocessing program or about the opportunities for cooperative R&D with NASA. He suggested several areas of investigation that might be of interest to him, but pointed out that his ability to follow through at this time was limited by a lack of funds.

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